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Mental Health in Dermatology: Addictions in Psoriasis and an Outlook on the Psychosocial Burden of Chronic Skin Diseases

vorgelegt von

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Affidavit

I, Maximilian Christian Schielein, hereby declare, that the submitted thesis entitled

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is my own work. I have only used the sources indicated and have not made unauthorized use of services of a third party. Where the work of others has been quoted or reproduced, the source is always given.

I further declare that the submitted thesis or parts thereof have not been presented as part of an examination degree to any other university.

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Maximilian Christian Schielein

Confirmation of congruency between printed and electronic version of the doctoral thesis

I, Maximilian Christian Schielein, hereby declare, that the submitted thesis entitled

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is congruent with the printed version both in content and format.

Munich, April 6th 2021

Maximilian Christian Schielein

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List of Abbreviations

BMG	Bundesministerium für Gesundheit (Federal Ministry of Health)
BVDD	Bundesverband der Deutschen Dermatologen (Association of the German Dermatologists)
CU	Chronic urticaria
DLQI	Dermatology Life Quality Index
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
HCP	Health care professional
MOOSE	Meta-Analysis of Observational Studies in Epidemiology
OR	Odds Ratio
PASI	Psoriasis Area and Severity Index
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-analyses report
WHA	World Health Assembly
WHO	World Health Organization

Publication List

Tizek L, **Schielein MC**, Zink, A. PeakPASI: A new measurement tool in psoriasis care. J Am Acad Dermatol 2020; [epub ahead of print]

Schielein MC, Tizek L, Schuster B, Ziehfreund S, Liebram C, Eyerich K et al. Always Online? Internet Addiction and Social Impairment in Psoriasis across Germany. J Clin Med 2020; 9(6):1818.

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Apendix List

Schielein MC, Tizek L, Knobloch L, Maaßen D, Bidermann T, Zink A. Psoriasis and addictions: assessing mental health in a cross-sectional study across Germany; [under review]

Schielein MC, Tizek, L, Ziehfreund S, Sommer R, Biedermann T, Zink, A. Stigmatization caused by hair loss – a systematic literature review. J Dtsch Dermatol Ges. 2020; [epub ahead of print]

Doctoral Thesis: Introductory Summary

Skin diseases are common throughout society and up to 60% of individuals are affected at any point in time (1). In general, they represent the fourth most common cause of non-fatal disease, and due to their morbidity, the burden of skin diseases is high (2, 3). Many skin diseases like psoriasis, chronic urticaria (CU), and alopecia are chronic in nature and require professional treatment. Psoriasis affects about 100 million individuals worldwide, and its prevalence in developed countries ranges from 1.5% to 5.0% (4), with a reported prevalence of 2.5% for Germany (5). In addition to many other comorbidities like psoriatic arthritis and cardio metabolic diseases, psoriasis is also associated with substantial mental burden (6). In 2014, psoriasis was identified as one of the five most impairing non-communicable diseases by the World Health Assembly (WHA) (7). Subsequently, the World Health Organization (WHO) issued and released the global report on psoriasis in 2016, which sheds light on the comprehensive burden of psoriasis (8).

Regarding the mental burden of skin diseases in general, a European study among 13 countries showed that people with skin diseases have an approximately twofold risk for depression and anxiety disorder compared to healthy individuals (9). For individuals with psoriasis, the risk is three times higher. Furthermore, several studies have found psoriasis to be associated with addictions (10–12). A meta-analysis suggested that patients with psoriasis have a pooled Odds Ratio (OR) of 1.78 for smoking in comparison to healthy controls (10). A systematic review suggested that alcohol consumption is higher among patients with psoriasis (11). However, evidence about other addictions hardly exists. Thus far, one monocentric study among 102 psoriasis patients indicated higher values for compulsive gambling and drug abuse in addition to a higher prevalence of smoking and alcohol dependency in patients with psoriasis compared to the general population (12). Other addictions, such as Internet addiction, have not yet been studied.

Along with the mental burden of the disease, the WHA and WHO emphasized the occurring stigmatization of psoriasis (7, 8). To illustrate the need for action, the WHO provided the example of a man who was ejected from a public pool due to other guest complaining about his psoriatic skin lesions. Despite knowing that the lesions were non-contagious, the lifeguards requested him to leave to satisfy the other guests (8). As psoriasis can cover any amount of body surface and any body localization including the genital and anal area, social impairments can occur in various situations, including very intimate situations such as sexual contact. While patients with psoriasis in general tend to have impaired quality of life and tend to avoid sexual contact, patients with genital

involvement report even poorer outcomes in both (13–15). Prevalence estimates for genital involvement are highly heterogeneous and range from 7% to 42% of all patients with psoriasis (16). Furthermore, 60% of affected patients from a French study indicated that they were aware of the genital involvement of their psoriasis; however, this genital involvement was not previously examined by an health care professional (HCP) (17). Affected individuals often hide this additional, personal, and very intimate burden rather than discuss it with their HCP, which could lead to an underestimation of the prevalence of genital psoriasis (17). However, despite effective treatments being available (15, 18), still many individuals with psoriasis do not seek medical care at all and therefore do not receive appropriate treatment (19).

Within their report, the WHO emphasized the importance of people-centered care approaches, especially for chronic skin diseases like psoriasis (8). The corresponding call for action addressing governments and policy makers included early detection as well as adequate medical treatment (8). Addressing HCPs, the WHO further emphasized the detection of psoriasis and comorbidities in all medical disciplines and the need to provide comprehensive care in multidisciplinary teams of specialists (e.g. dermatologists, rheumatologists, psychologists) using a holistic approach (8, 20). Another call for action of the WHA resolution addressed all member states directly and demanded to raise awareness for the psychosocial burden of psoriasis (7). Therefore, prevention programs should be implemented to reduce stigmatization, which had been identified as a major factor for mental burden in chronic skin diseases. These programs ideally have the potential to be extended to other visible skin manifestations like atopic dermatitis, alopecia, and CU, which all are accompanied by a substantial burden (2, 21–23). One example for the implementation of this demand is a nationwide task force founded by the Federal Ministry of Health (Bundesministerium für Gesundheit; BMG) in Germany, which aimed to widen the horizon of dermatological research and focus to not only include psoriasis, but include all visible skin diseases and their potential stigmatization (24, 25).

Subsequently, the aim of this doctoral thesis was to follow the WHO’s call for action and to further characterize the mental burden of chronic skin diseases. This thesis therefore focused on (I) addictions in psoriasis, especially Internet addiction, using both patient-physician settings and a people-centered care approach, (II) genital psoriasis and sexual avoidance, and (III) stigmatization of people with alopecia as part of a nationwide BMG project and as an outlook for diseases other than psoriasis.

Psoriasis and addictions: assessing mental health in a cross-sectional study across Germany (Appendix I)

While many studies suggested a high prevalence of alcohol dependency and cigarette smoking in patients with psoriasis (9–11, 26, 27), Zink et al. performed the first study that investigated further addictions in a single-center study and revealed a high positive screening rate for compulsive gambling and drug abuse in 102 patients with psoriasis (12). Subsequently, the aim of this study was to estimate the prevalence of six common addictions (smoking, alcohol, gambling, Internet, food, and drugs) among patients with psoriasis to generate findings in a multi-center approach across Germany. Additionally, clinical factors associated with the occurrence of the respective addictions were to be identified, which were thought to function as indicators of poor mental health in time-restricted clinical practice.

In this cross-sectional study, 32 dermatological practices and 4 dermatological clinics across south-western Germany recruited a total of 502 patients (mean age: 49.7 ± 14.6 years; 43.4% women) between September 2018 and November 2019. Screenings for all mental health outcomes were performed using standardized and validated questionnaires and a one-question item on tobacco smoking. First findings by Zink et al. were confirmed, and positive screening rates for pathological gambling and drug abuse exceeded those reported for the general population (gambling: 1.2% vs. 0.2% (28); drug abuse: 6.0% vs. 3.2%-5.2% (29)). Furthermore, the rate of positive screenings regarding Internet addiction was higher than in a representative sample of German adolescents (3.8% vs. 3.2%) (30). This rate was surprisingly high considering that Internet addiction decreases with rising age (31, 32) and that the participants' mean age in this study (49.7 years) was considerably higher than the participants' mean age in the comparison study (14.9 years). With limited time per patient in clinical practice, the second aim of this study was to identify certain influencing factors for the occurrence of the respective addictions. Younger age was associated with a higher chance for the occurrence of most addictions. Other associated factors were however inconsistent. Therefore, standardized and not too time-consuming assessments of mental comorbidities might be of high value for future psoriasis care.

This study was also used to test the hypothesis of a pervious published study (12). As the 'Psoriasis Area and Severity Index' (PASI), the most common used measurement to assess the characteristics of psoriasis, only represents disease severity at one time point, it might not be conclusive for a lifetime burden, which potentially cumulate throughout patients' medical history

(33, 34). Therefore, we aimed to determine the association of patients highest ever documented PASI, the 'PeakPASI', and patient reported outcomes.

PeakPASI: A new measurement tool in psoriasis care

All participating dermatologists were asked to provide the PeakPASI for each patient. Overall, PeakPASI values for 398 patients were recorded. To assess differences in the study population, two PeakPASI thresholds were chosen: ≥10, based on clinical practice and ≥13.6, based on a median split. According to the median split-based analyses, patients having a higher PeakPASI were more likely to show higher 'Dermatology Life Quality Index' (DLQI) values, indicating higher disease related impairment of quality of life, and lower values of heuristic happiness. Even though, the PeakPASI holds some limitations, this letter represents the first report trying to evaluate its potential and to improve comprehensive and patient-centered disease characterization by including a measure for lifetime disease burden.

As a result of the main subject of this study, Internet addiction was found to be of enormous interest. This rising phenomenon of our century was only recently added to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) as the most potent problem in need of further research and it is showing rising trends with the omnipresence of the Internet and online possibilities (35, 36). As this first study was carried out in a typical medical setting and only considered patients who were in medical care, the study partially neglected the principle of people-centered care demanded by the WHO. Therefore, the second study of the Ph.D. thesis was performed to access individuals who may be neglected by more conventional study methodologies. This study also investigated Internet addiction in conjunction with established addictive comorbidities (alcohol dependency and tobacco smoking) in a more diverse sample of individuals with psoriasis.

Always Online? Internet Addiction and Social Impairment in Psoriasis across Germany

To reach affected individuals, a cross-sectional online survey was designed in collaboration with the online self-help organization 'Psoriasis Netz,' which provides up-to-date information on psoriasis and related topics. The questionnaire was shared via the self-help organization's newsletter, webpage, and social media channels, including Facebook and Twitter. Additionally, it was distributed via the patient organization 'Farbenhaut' and a campaign of the Association of the German Dermatologists (Berufsverband der Deutschen Dermatologen; BVDD) called 'Bitte berühren.' This method was used to reach individuals who (i) were affected by psoriasis and (ii)

felt the need for further support and therefore turned to a respective entity. To further emphasize the people-centered nature of this investigation and acknowledge potential psychological components of Internet addictions (37), information about the social impairment of participants as well as activities avoided due to psoriasis was collected.

Overall, 460 individuals (mean age: 45.9±13.7 years; 62.4% women) participated in this study. Of these, 22.8% indicated to do not utilize medical health care at the time of study participation and 88.3% stated to be at least rarely socially impaired. When considering leisure activities, participants with psoriasis most frequently stated swimming as the activity from which they abstained the most. As this is in line with first findings reported in the 1980's (38), these results emphasize the need for interventions such as those planned and conducted by the aforementioned BMG initiative and the importance of reducing stigmatization (24). Free text answers like avoiding 'Any activity requiring short clothing' (woman; 21 years) or 'Roughhousing with my son' (man; 34 years) furthermore underlined the substantial individual burden under which affected individuals often suffer.

The positive screening rate for Internet addiction was 8.5%. This was substantially higher than the positive screening rates reported in the first conducted study and in the literature on the German general population (3.8% vs. 1.0-1.5% (31)). As this study was based on an online approach, one could have anticipated higher positive screening rates, as affected individuals without Internet access were not able to participate. However, a prior study on 245 healthy individuals recruited in an online setting also revealed a prevalence of only 1.2% (39), which increases the meaningfulness of our data among individuals with psoriasis.

Furthermore, 40.0% of participants had positive screenings for depression, 17.1% for alcohol dependency, and 32.6% for daily smoking. When compared to the first study of this thesis and to the general population, respectively, results for smoking were comparable to the results in psoriasis patients in clinics and practices (32.6% vs. 30.3% vs. 15.1% (29)). In contrast, alcohol dependency was found to be more prevalent than in psoriasis patients reported before and the general population (17.1% vs. 8.6% vs. 3.1% (29)). The positive screening rate of depression slightly exceeded previous questionnaire-based findings among patients with psoriasis (40.0% vs. 13.8-39.2% (27)).

While the approach of this study mainly targeted people who subscribed to newsletters or social media channels of certain webpages or who visited the self-help organization's website during the study period, another online study that included short versions of screening questionnaires for

Internet addiction and depression was conducted. As many individuals search for health-related information using search engines (40–43) or social media (44), we decided to target individuals who recently searched for psoriasis or CU using advertisements on Google and Facebook. People with CU were also included in the study, as it is an additional chronic inflammatory skin disease that affects 0.5% of the general population in Europe (45) and is also accompanied by a high mental burden (21, 22). No data on Internet addiction was available for CU so far.

People-centered care for psoriasis and urticaria: Are we overlooking Internet addiction while only considering patients and physician settings?

This cross-sectional study comprises self-reported data from individuals with psoriasis and CU living in Germany using an online survey advertised via Facebook and Google from December 2018 to January 2019.

Overall, 1,686 participants (mean age: 36.9 ± 12.9 years; 74.0% women; 38.5% having psoriasis) were included in this study. More than half of the participants (54.7%) were currently not receiving medical care for their skin disease, with substantially more individuals with CU currently not utilizing medical care (60.3% vs. 45.9%; $p<0.001$). This proportion was considerably higher than in the third study of this thesis. Overall, 16.0% of participants were screened positive for Internet addiction. This positive screening rate again exceeded that of the online study among individuals reached via self-help groups for psoriasis (8.5%) as well as the positive screening rate among the multi-center study of patients with psoriasis (3.8%) and that of a representative sample of more than 8,130 individuals living in Germany (1.0-1.5%) (31). The inherent characteristics of an online approach might explain the higher positive screening rates in this sample and the sample of participants from an online self-help group. This potential effect, however, was as previously mentioned partly invalidated by Eichelberg et al., who found a prevalence for Internet addiction of only 1.2% among regular Internet users who were recruited, among others, from Facebook (39). This prevalence in turn does not exceed the results for the general German population, which might indicate that individuals with chronic skin manifestation are more likely to be affected by Internet addiction. A comparison of the positive screening rates in the three conducted studies furthermore suggests that individuals reached online might have a greater disease burden than those individuals seen in dermatological clinics and practices.

The results illustrate that the mental burden of individuals affected by psoriasis is high and that addictions, especially Internet addiction, are common among affected individuals. However, this

already high burden of disease increases when the genital area of individuals is affected (13–15, 46). Meanwhile, information on affected individuals outside of a conventional patient-physician setting is nonexistent. Furthermore, previous studies focused on the presence of intimacy avoidance without further qualitative analyses of respective reasons for avoidance. For example, a European cross-sectional study used only one question within the DLQI, stating 'Over the last week, how much has your skin caused any sexual difficulties?' and thus neglecting individual reasons for avoidance (9). Subsequently, the aims of the next study were to investigate the occurrence of genital psoriasis in a non-clinical setting and to determine factors related to the avoidance of sexual activities due to psoriasis.

Genital Psoriasis and Associated Factors of Sexual Avoidance – A People-centered Cross-sectional Study in Germany

This article was published in *Acta Dermato-Venereologica* (ISI Citation Report 2019: Impact factor: 4.016, Ranking: 7/68 [Dermatology]), where it was selected as a 'research highlight of the month,' and subsequently featured in their monthly newsletter (05/2020). The recruitment was carried out mostly via the patient self-help organization 'Psoriasis-Netz' and other institutions from March to June 2019 using a similar methodology as the one described in the second project of this thesis.

Overall, 344 individuals with psoriasis participated (mean age: 44.6 ± 13.2 years; 59.3% women). Of those, 83 (24.1%) did not currently utilize medical care and 198 (57.6%) stated that their genital area was affected. Compared to the prevalence reported in the literature (7-42%) (16), the occurrence of genital psoriasis was considerably higher in this study. In our study, individuals with genital psoriasis also more frequently reported pain (58.6% vs. 26.0%; $p<0.001$) and avoidance of sexual activities because of their psoriasis (74.2% vs. 52.7%; $p<0.001$) than those without genital involvement. In line with the limited preexisting literature (46, 13), the most common reason for avoiding sexual activities was shame, followed by pain and the fear of rejection. However, the presence of shame as the most common category implies that focusing on the stigmatization of skin lesions, especially in areas that highly affect individuals' private life, might be beneficial for future people-centered care in psoriasis. Additionally, this study underlined the role of patient organizations in reaching out to highly vulnerable patient groups and individuals who do not seek medical help while promoting people-centered care.

Finally, as an outlook for skin manifestations which should be further considered with regard to stigmatization and social withdrawal and as part of the aforementioned BMG-project (24), a systematic review on stigmatization in individuals with alopecia was conducted.

Stigmatization caused by hair loss – a systematic literature review (Appendix II)

The aim of this additional paper in the scope of the thesis was to systematically summarize existing literature on the stigmatization of hair loss. Alopecia can be present as a symptom due to different pathogeneses and has varying severities (47–49). The most common forms of alopecia are androgenetic alopecia and alopecia areata (47). Additionally, hair loss is a common side effect of cancer treatments (49). According to the WHA resolution (7), psoriasis was selected as a model disease for planning interventions, which would then to be expanded to include other skin diseases. This literature review generated significant attention within the BMG's project initiative, as it was the first review on further dermatological diseases to be conducted, finished, and published.

Stigmatization describes a phenomenon that excludes affected individuals from total social acceptance (50). This problem can be triggered by the patients themselves (internal stigma) or be induced by their environment (external stigma) (50, 51). With regard to the social stigmatization of dermatological diseases, society's point of view may be biased. While analyzing dermatologic findings among all-time top 10 American film villains and heroes, it appeared that substantial skin alterations were only present in villains (52). Subsequently, three out of ten villains showed substantial signs of alopecia, and this characterization of evil characters using alopecia dates as far back as 1921 in the film *Nosferatu* (53). Further examples for notable alopecic villains include Dr. Hannibal Lecter (*The Silence of the Lambs*; 1991), Dr. Evil (*Austin Powers in Goldmember*; 2002), and Lord Voldemort (*Harry Potter*; 2005-2011). While this association is only exemplary, it might contribute to prejudice and stigmatization, which in turn can lead to reduced mental health and severely impair the quality of life of affected individuals (25, 54). To generate evidence-based knowledge about stigmatization in hair loss, the presented systematic review was planned thoroughly in accordance with the respective *'Preferred Reporting Items for Systematic reviews and Meta-analyses report'* (PRISMA) (55) and *'Meta-Analysis of Observational Studies in Epidemiology'* (MOOSE) guidelines (56), and was registered within the PROSPERO database (Identification number: CRD42019122966) (57).

Within four databases on medical and psychological scientific literature, 98 publications were identified and entered the screening. After reviewing the publications, 11 articles were included in the review. The identified studies showed a high degree of heterogeneity. Five articles investigated therapy induced alopecia after preexisting cancer, four androgenetic alopecia, three alopecia areata, and one diffuse alopecia. Only four studies shared a common questionnaire for the quantification

of stigmatization; the *'Hairdex'* (58). In combination with the high heterogeneity and partly flawed methodological approaches by different authors, evidence on stigmatization due to alopecia was weak and difficult to compare. Single studies, however, stated perceived stigma of hair loss to be similar to the stigma of psychiatric conditions (59) and more severe than that of vitiligo (60). Although the resulting psychological stress is very high for those affected, stigmatization is often considered as one of many factors that impair quality of life. Overall, the review showed that specific studies on stigmatization in hair loss are rare and that longitudinal studies are non-existent, although they are strongly recommended.

In summary, this Ph.D. thesis contributes to the fundamental characterization of the mental burden of chronic skin diseases, with a focus on psoriasis. It introduced Internet addiction as a possible addictive comorbidity and demonstrated high impairment in chronic skin diseases, particularly in genital psoriasis. Future studies should seek to validate these findings using claims data or suitable control groups. Standardized routine screening could be introduced to detect potential mental health impairments. Additionally, the thesis introduced a measure for disease severity beyond the conventional PASI, the PeakPASI. Even though, it includes limitations, this additional measure has the potential to better characterize disease burden that might accumulate throughout the disease history. Furthermore, the studies of this thesis represent one of the first approaches that focused on people-centered health care in chronic skin diseases as demanded by the WHO. Individuals reached using people-centered approaches showed a substantially higher rate of positive screenings for mental comorbidities than participants recruited from a traditional medical setting. Outreach programs and patient-journey approaches that are personalized and that contact affected individuals in the context of their everyday lives represent a highly promising approach when considering the possibilities of mental burden reduction in individuals affected by chronic skin diseases. Moreover, by exploring the stigmatization of alopecia, the thesis included evidence-based groundwork on another highly stigmatized chronic skin disease. Altogether, the thesis illustrates how chronic skin disorders can influence mental health and that further information on possible psychological comorbidities, like addictions, needs to be covered in future research including patient- and people-centered health care approaches.

Specification of the personal contribution

For the first study and Appendix I, I was responsible for the conceptual design, adaptation according to the comments from all co-authors and my thesis advisory committee, designing a

suitable data protection model, preparing and reaching an ethical approval, and contacting over 200 dermatologists. Furthermore, contracts with all 35 centers had to be implemented. I coordinated all reception of data, payments, data digitalization and validation, data analysis, and preparation of the first manuscript. Lastly, all coauthors revised the manuscript and I submitted it. For the first manuscript, Dr. Linda Tizek and I handled all data analysis and writing likewise, wherefore we shared the first authorship.

For the second and fourth study, I was responsible for the initial founding of the cooperation with the involved patient self-help group, 'Psoriasis Netz'. After several discussions, I created a conceptual study design and adapted it according to the reviews by the patient organization and our working group. Furthermore, I obtained ethics committee approval and programmed the online questionnaire together with Barbara Schuster. After data collection, I was responsible for the data preparation, statistical analyses, and writing of the initial manuscript as well as submission of the final version that was approved by all co-authors.

In the third study, my contributions included conceptual design and data analysis. I further wrote the first draft of the manuscript, adapted it to all coauthors' comments, and submitted it.

For the systematic review (Appendix II), I was responsible for planning the review, defining and amending the search terms, defining the inclusion and exclusion criteria, and preparing and registering the review protocol. Furthermore, I was responsible for applying the search terms, extracting and sorting all data, removing duplicates, and preparing titles, abstracts, and full papers for screening and evaluation. I conducted the screening of all abstracts, titles, and full publications. I systematically reviewed all publications and evaluated them according to the respective guidelines that I defined in the study protocol. I compared them with those of Dr. Linda Tizek and created the first draft of the final publication, which I amended according to all comments of the co-authors.

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Publication I: PeakPASI: A new measurement tool in psoriasis care

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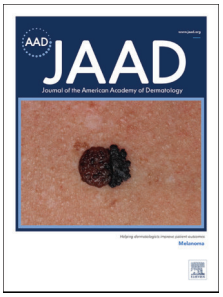

PeakPASI: A new measurement tool in psoriasis care

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Title: PeakPASI: A new measurement tool in psoriasis care

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Dear Editor: Psoriasis can impair happiness and quality of life,[1] with people having a longer disease duration and a more severe psoriasis showing higher impairment.[2] The 'Psoriasis Area and Severity Index' (PASI) is a commonly used measuring tool, but it represents only a snapshot of a single visit. Accordingly, important factors like treatment outcomes or the individual lifetime burden may not be fully reflected.[3,4] Thus, we suggest to implement a stable long-term score and to use the highest ever documented PASI, the 'PeakPASI'.[5]

To test its feasibility, a cross-sectional study including psoriasis patients aged ≥18 years from 36 dermatological settings was performed in Germany between 09/2018 and 11/2019. Dermatologists were asked to recruit patients consecutively with any severity and to report their PeakPASI documented in the patient's file. Additionally, patients answered questions on 'Dermatological Life Quality Index' (DLQI) and happiness.[1] To assess differences in patients, two classifications were calculated: (i) PeakPASI <10/≥10; (ii) PeakPASI <13.6/≥13.6, based on a median split.

Overall, 398 patients (mean age 49.1 ± 14.5, 42.5% women) were included (Table 1, Supplementary Table 1: https://data.mendeley.com/datasets/2jxyvxw6t8/3). At study examination 302 patients had a higher PeakPASI than PASI. In both classifications, people with a higher PeakPASI were more likely to be male, to have a higher PASI, to receive systemic treatment, and to have previously received UV therapy (Table 1, Supplementary Table 2: https://data.mendeley.com/datasets/2jxyvxw6t8/3). Additionally, people having a PeakPASI ≥13.6 had significantly higher DLQI and lower happiness (Figure 1).

The mean value of PeakPASI was twice as high as the mean PASI, indicating that the cumulative burden is likely to be higher than one snapshot at a specific moment could depict. The PeakPASI might also be important when thinking about future treatment options and their effectiveness as people with a higher PeakPASI were more likely to having received a higher number of previous systemic treatments. Possible explanations for that might be that people with a certain PeakPASI value have delayed responses to treatment, need early changes of treatment more often, were off

treatment when the PeakPASI was documented, or that they did not adhere to the prescribed treatment.

One limitation is that the PeakPASI is a rather theoretical approach. It is not routinely documented and information about the real highest lifetime PASI may get lost as patients consult several physicians which generally could be prevented by using electronic health records accessible for all treating physicians. In this pilot study a few important factors were not considered: status of treatment when PeakPASI was measured, time since onset of psoriasis, time span between PASI and PeakPASI, time span during which PeakPASI was documented, intervals at which patients were seen, duration of current treatment. Additionally, in some patients with a generally mild psoriasis a high PeakPASI might be measured during a severe flare, which would overestimate the effect.

Future research should examine factors like after which length of time a change of therapy was initiated and whether the PeakPASI is helpful in determining the need for more comprehensive therapies.

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Figures and Tables

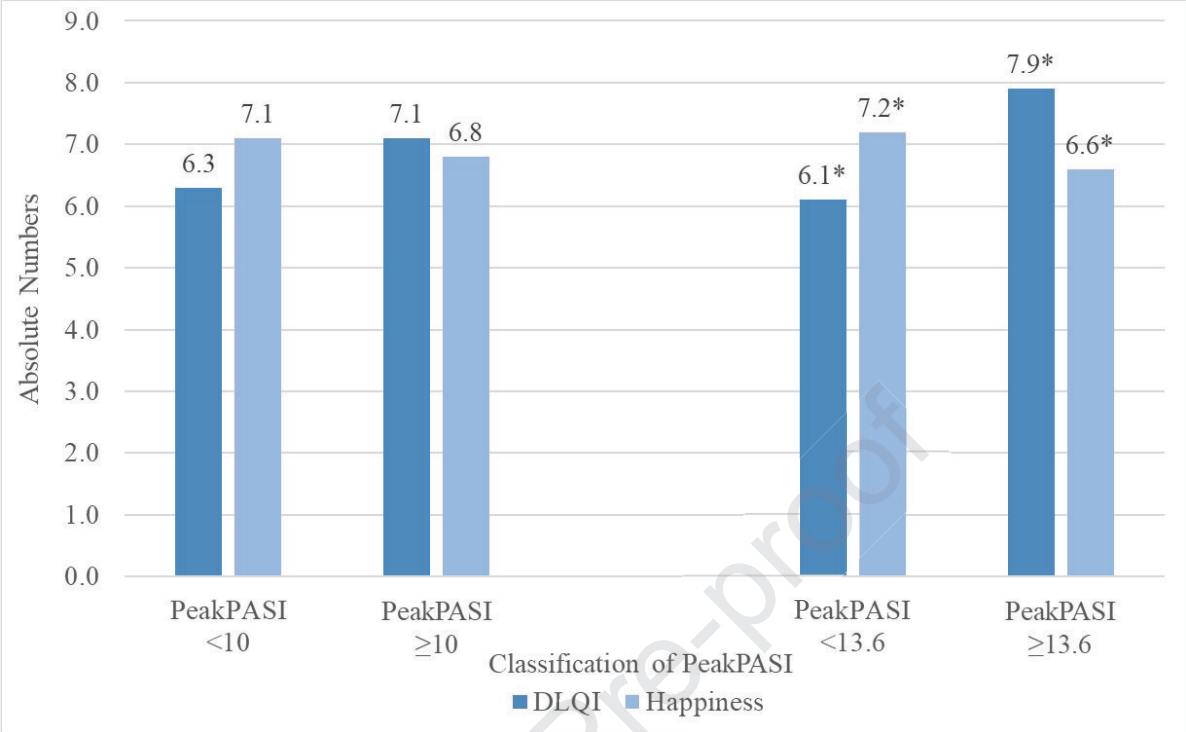
Figure 1. Psoriasis. DLQI and happiness in the study population classified by two PeakPASI thresholds

PeakPASI = highest ever documented PASI, DLQI = Dermatology Life Quality Index (higher values represent a lower perceived quality of life); happiness = heuristic happiness (higher values mean higher happiness), * significant at alpha < 0.005

Table 1: Patient's characteristics separated by a PeakPASI ≥10 as well as by the median PeakPASI of 13.6.

	Total (n=398)	**PeakPASI <10 (n=92)**	**PeakPASI ≥10 (n=306)**	**PeakPASI <13.6 (n=197)**	**PeakPASI ≥13.6 (n=201)**
Age (mean ± SD)	49.1 ± 14.5	49.7 ± 14.7	48.9 ± 14.4, p=0.649	48.2 ± 14.1	50.0 ± 14.9, p=0.213
Gender					
Female	169 (42.5%)	58 (55.8%)	111 (37.8%), **p=0.001**	96 (48.7%)	169 (36.3%), **p<0.001**
Male	229 (57.5%)	46 (44.2%)	183 (62.2%)	101 (51.3%)	229 (63.7%)
PASI					
Mean	7.3 ± 7.7	3.3 ± 2.6	8.5 ± 8.3, **p<0.001**	4.6 ± 4.0	9.9 ± 9.5, **p<0.001**
Range	0 – 53.8	0.0 – 9.9	0.0 – 53.8	0.0 – 13.0	0.0 – 53.8
PeakPASI					
Mean	15.4 ± 9.2	5.8 ± 2.6	18.3 ± 8.4, **p=0.001**	9.0 ± 3.5	21.8 ± 9.2, **p<0.001**
Range	0.1 – 53.8	0.1 – 9.9	10.0 – 53.8	0.1 – 13.5	13.6 – 53.8
DLQI	7.0 ± 6.8	6.3 ± 6.7	7.2 ± 6.8, p=0.341	6.1 ± 6.2	7.9 ± 7.3, **p=0.010**
Happiness	6.9 ± 2.0	7.1 ± 1.9	6.8 ± 2.0, p=0.355	7.2 ± 1.9	6.6 ± 2.0, **p=0.005**
Current UV therapy	47 (11.8%)	4 (4.3%)	43 (14.1%), **p=0.011**	19 (9.6%)	28 (13.9%), p=0.185
Number of current systemic therapies					
0	142 (35.7%)	43 (46.7%)	99 (32.4%), **p=0.002**	79 (40.1%)	59 (29.4%), **p=0.030**
1	256 (62.6%)	49 (53.2%)	211 (69.0%)	118 59.9%)	142 (70.7%)
Current Conventional Therapy	98 (24.6%)	17 (18.5%)	81 (26.5%), p=0.119	45 (22.8%)	53 (26.4%), p=0.414
Current Apremilast Therapy	16 (6.3%)	3 (3.3%)	13 (4.2%), p=0.672	7 (3.6%)	9 (4.5%)
Current TNF – Alpha Therapy	37 (9.3%)	8 (8.7%)	29 (9.5%), p=0.821	15 (7.6%)	22 (10.9%), p=0.253
Current IL-17 Therapy	69 (17.3%)	18 (19.6%)	51 (16.7%), p=0.520	34 (17.3%)	35 (14.4%), p=0.968
Current IL-23 Therapy	30 (7.5%)	5 (5.4%)	25 (8.2%), p=0.384	15 (7.6%)	15 (7.5%), p=0.954
Other biologics	12 (3.0)	1 (1.1%)	11 (3.6%), p=0.217	5 (2.5%)	7 (3.5%), p=0.582
Previous UV Therapy	61 (15.3%)	3 (3.3%)	58 (19.0%), **p<0.001**	21 (10.7%)	40 (19.9%), **p=0.011**
Number of previous systemic therapies					
0	193 (48.5%)	49 (53.3%)	144 (47.1%), p=0.287	107 (54.3%)	86 (42.8%), **p=0.015**
1	95 (23.9%)	21 (22.8%)	74 (24.2%)	41 (20.8%)	54 (26.9%)
2	57 (14.3%)	13 (14.1%)	44 (14.4%)	30 (15.2%)	27 (13.4%)
≥ 3	53 (13.4%)	9 (9.8%)	44 (14.4%)	19 (9.6%)	34 (17.0%)

SD = Standard deviation; PASI = Psoriasis Area and Severity Index; PeakPASI = highest ever documented PASI; DLQI = Dermatological Life Quality Index (higher values represent a lower perceived quality of life), happiness = heuristic happiness (higher values represent a higher happiness); other biologics = for example include patients that are part of a double-blind trial; Ustekinumab was included into the category of IL-23 therapies.



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Always Online? Internet Addiction and Social Impairment in Psoriasis across Germany

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Abstract: With the World Health Organization (WHO) demanding further investigation of the social impairment and psychosocial burden of psoriasis, a first study identified a high prevalence of Internet addiction. The aim of this study was to assess social impairment and estimate the occurrence of Internet addiction along with depression, cigarette smoking, and alcohol dependency in individuals with psoriasis recruited online in a people-centered care approach. A cross-sectional online survey was carried out across Germany between March 2019 and June 2019. The questionnaire contained information on social impairment, smoking habits, as well as validated questionnaires on Internet addiction, depression, and alcohol dependency. Overall, 460 individuals (62.4% female; mean age: 45.9 ± 13.7 years) with psoriasis were included. Of those, 406 (88.3%) stated to be at least rarely socially impaired. The positive screening rate for Internet addiction was 8.5%. Furthermore, 40.0% had positive screenings for depression, 17.1% for alcohol dependency, and 32.6% for daily smoking. Positive screenings for Internet addiction and alcohol dependency were substantially more frequent in individuals with psoriasis than in the German general population. In order to meet the demands of the WHO, Internet addiction could be considered as a potential comorbidity in psoriasis and a focus on people-centered care is advisable for further research.

Keywords: psoriasis; Internet addiction; people-centered care; social impairment; stigmatization

1. Introduction

Internet addiction is a phenomenon first appearing at the turn of the millennium that has since then begun to rise immensely in importance [1]. It was classified as the most potent problem within the revised Diagnostic and Statistical Manual of Mental Disorders (DSM) in 2013 [2]. In Germany, prevalence estimations range from 1.0% in the general population up to 3.2% in the subgroup of adolescents [3,4]. With regard to skin diseases, a recent study found that pathological Internet use and Internet addiction were substantially more frequent among a sample of 502 patients with psoriasis (3.8%) than in the general population (1.0%) [3,5].

Psoriasis is a chronic inflammatory skin disease affecting 1.2–3% of individuals in Germany [6–8]. Patients often have an impaired quality of life and reduced happiness [8,9]. Individuals with psoriasis

tend to avoid or reduce physical activities and often withdraw themselves from social activities [10,11] and intimate contact [12,13]. These social impairments are broadly individual for each patient and associated with various comorbidities [14]. Patients often suffer from a psychosocial burden due to stigmatization [15,16] as well as from comorbidities such as depression and addictions [17,18]. Subsequently, the World Health Organization (WHO) emphasized the importance of recognizing the stigmatization in psoriasis and its potential consequences for burden of disease and mental comorbidities [19]. While reviews indicate more frequent alcohol dependency and cigarette smoking in psoriasis patients [20,21], evidence on compulsive Internet use and Internet addiction remains limited to one study [5].

If treated appropriately, patients with psoriasis can benefit from highly effective therapies. Individuals treated effectively tend to have not only less severe skin lesions but also reduced depressive symptoms and social impairment [22,23]. The reduction of comorbidities and the promotion of mental health of individuals with psoriasis are essential according to the WHO [19]. However, not all patients receive therapies as recommended by guidelines [24,25], and, since not all affected individuals seek medical care, many affected individuals are not considered as psoriasis patients [26]. Hence, the WHO demands to focus on people-centered instead of patient-centered health care [27,28]. Despite this, most research still focuses on registries including mainly, moderately, and severely affected individuals and typical patient settings such as dermatological practices and clinics. To reach individuals outside of conventional settings, online approaches can be beneficial [13,29] as many individuals, regardless of contact to a physician, search for health-related information online [30–33].

The aim of this study was therefore to assess social impairment and to estimate the occurrence of Internet addiction along with depression, smoking, and alcohol dependency among individuals with psoriasis using a people-centered online approach.

2. Experimental Section

2.1. Study Design and Recruitment

This cross-sectional study was carried out as an online survey among individuals with psoriasis in Germany from March to June 2019. The online questionnaire was distributed via an online self-help platform "Psoriasis-Netz", a patient online platform "Farbenhaut" as well as a national campaign of the "Association of the German Dermatologists" (BVDD). The project was most promoted by "Psoriasis-Netz" on their website together with current information for individuals interested in psoriasis. Its monthly e-mail newsletter was sent to 2296 registered individuals across Germany. "Farbenhaut" and the BVDD shared the questionnaire on their social media channels one month before completion of recruitment for the study.

Only individuals who stated having psoriasis diagnosed by a physician were included in the analyses. Additional exclusion criteria were the presence of implausible data or more than 20% of missing values. Electronic informed consent from each participant was acquired prior to study inclusion. All study procedures were in accordance with the Declaration of Helsinki and were reviewed as well as approved by the local ethics committee of the Technical University of Munich (reference 25/19 S).

2.2. Questionnaire

The study questionnaire was developed in collaboration with "Psoriasis-Netz". One dermatologist, two epidemiologists, and two members of "Psoriasis-Netz" were involved in the process. Questions were only added if they were accepted unanimously. The questionnaire was pre-tested by three researchers and three individuals affected by psoriasis and adapted according to their comments.

Participants answered questions on sociodemographic variables and their medical history, including age, gender, disease severity in general and at time of participation (self-classification as "mild", "moderate", or "severe", respectively) as well as disease duration and current utilization of

medical care. Due to the nature of the chosen online approach, standardized reflection of disease severity using physician-based Psoriasis Area and Severity Index (PASI) or body surface affected (BSA) was not possible. In order to keep the questionnaire concise, social impairment was assessed with a one-question item asking "Does your psoriasis prevent you from pursuing certain leisure activities?", which could be answered on a five-point Likert scale ranging from "never" to "always". Participants who stated that their psoriasis prevents them from taking part in certain leisure activities were asked for the main restrictions using free-text comments. After revising the questionnaire, examples for possible answers were added ("e.g., swimming, sauna, sunbathing, ... ").

Internet addiction was assessed using the Compulsive Internet Using Scale (CIUS; Cronbach's $\alpha = 0.93$) [34,35]. The questionnaire comprises 14 questions, which are to be answered on a five-point Likert-scale ranging from "never = 0" to "very often = 4". Subsequently, the score ranges from 0 to 56. A cutoff score of 21 was used to estimate the prevalence of Internet addiction [5,35]. Additionally, participants were asked to state the days per week and hours per day spent online in their leisure time.

Depressive behavior was assessed with the International Classification of Diseases (ICD)-10-based WHO-Five Well-Being Index (WHO-5, Cronbach's $\alpha = 0.88$) [36,37], a widely used, validated questionnaire comprising five questions on well-being. Answers range from "never" to "always" and are rated from zero to five, respectively. The resulting sum is multiplied by four, resulting in a score between 0 and 100. A cutoff value of ≤28 for depression showed a sensitivity of 0.94 and a specificity of 0.83 and, therefore, was used to determine depression as a study outcome [38].

To screen for alcohol use disorder, the DSM-based CAGE-questionnaire was used [39]. It comprises questions on "cutting down", "annoyed by criticism", "guilt about drinking", and alcohol as an "eye-opener" in the morning. Questions are answered with "no" or "yes". The subsequent score ranges from zero to four. The instrument showed good test-retest reliability (0.80–0.95) and the cutoff value of at least two questions answered with "yes" as a positive screening for alcohol use disorder previously showed a sensitivity of 0.71 and a specificity of 0.90 [40].

Smoking was assessed by one question: "Do you smoke cigarettes?". Participants who stated that they "never" or "seldom" smoke were classified as non-smokers. Participants who stated that they smoke daily, regardless of the stated amount, were considered smokers.

2.3. Statistical Analyses

As the online method of patient recruitment of this people-centered survey was explorative, study size was determined by the number of individuals recruited during a three-month time frame. Descriptive data were computed for all participants and stratified by social impairment. Group differences were calculated using unpaired t-tests or chi-square tests. Prevalence of positive screenings for Internet addiction along with those for depression, smoking, and alcohol dependency were determined. Results were stratified by gender, age (by median split; 46 years), and social impairment. To avoid confounding, possible influencing factors were assessed using univariate and multiple regression models. All factors that showed a significant association in the univariate analysis, were entered in the multiple regression model with backward selection. Independent variables included age, gender, disease duration, utilization of medical care, disease severity at time of study participation, severity in general, and social impairment. Odds ratios (OR) and respective 95% confidence intervals (95% CIs) were calculated. To analyze activities avoided due to psoriasis, free-text answers were categorized using an inductive analyzing procedure. Categories were descriptively quantified. Additionally, quantities of the 50 most commonly used words were visualized while excluding nonspecific words such as "I", "with", or "do". IBM SPSS Statistics (Version 25, IBM Corporation, Armonk, NY, USA) was used for all analyses and alpha was set at 0.05.

3. Results

A total of 466 individuals with psoriasis participated in this study. Of these, six were excluded due to implausible data, resulting in a total of 460 participants being analyzed. The mean age was

45.9 ± 13.7 years and 62.4% (n = 287) of the participants were female. The mean duration of disease was 21.0 ± 14.7 years and 22.8% (n = 105) of the participants were currently not in medical care. About half of the participants stated to have a moderate disease severity both at the time of study participation (55.0%; n = 253) and in general (56.3%; n = 259). When comparing general and current disease severity, 32.8% (n = 151) of the participants stated that their psoriasis was better at the time of study participation, while 13.0% (n = 60) indicated a worse disease severity (Table 1).

Table 1. Characteristics of study participants in total and stratified by influence of psoriasis on avoiding free-time activities.

	Total (n = 460)	**Psoriasis is Preventing Leisure Activities**		***p*-Value**
		Never or Rarely (n = 130)	**Sometimes, Frequently, or Always (n = 330)**	
		Age (years)		
(Mean, SD)	45.9 ± 13.7	46.7 ± 14.1	45.6 ± 13.6	0.426
Age group <46	222 (48.3%)	62 (47.7%)	160 (48.5%)	0.878
Age group ≥46	238 (51.7%)	68 (52.3%)	170 (51.5%)	
		Gender; n (%)		
Female	287 (62.4%)	86 (66.2%)	201 (60.9%)	0.296
Male	173 (37.6%)	44 (33.8%)	129 (39.1%)	
		Duration of psoriasis (years)		
(Mean, SD)	21.0 ± 14.7	21.9 ± 15.1	20.7 ± 14.6	0.416
		Currently in medical care; n (%)		
Yes	355 (77.2%)	95 (73.1%)	260 (78.8%)	0.189
No	105 (22.8%)	35 (26.9%)	70 (21.2%)	
		Severity at the time of study participation; n (%)		
Mild	102 (22.2%)	47 (36.2%)	55 (16.7%)	<0.001
Moderate	253 (55.0%)	74 (56.9%)	179 (54.2%)	
Severe	105 (22.8%)	9 (6.9%)	96 (29.1%)	
		Severity in general; n (%)		
Mild	37 (8.0%)	22 (16.9%)	15 (4.5%)	<0.001
Moderate	259 (56.3%)	83 (63.8%)	176 (53.3%)	
Severe	164 (35.7%)	25 (19.2%)	139 (42.1%)	
		Severity at study participation compared to severity in general; n (%)		
Worse	60 (13.0%)	12 (9.2%)	48 (14.5%)	0.225
Equal	249 (54.1%)	77 (59.2%)	172 (52.1%)	
Better	151 (32.8%)	41 (31.5%)	110 (33.3%)	

SD = standard deviation.

3.1. Social Impairment

Overall, 330 (71.7%) stated that their psoriasis at least sometimes prevents them from certain leisure activities. Of these, 124 (27.0%) individuals answered this question with "frequently" and 92 (20.0%) with "always". Participants indicating that their psoriasis prevents them at least sometimes from certain leisure activities reported a higher rate of severe disease characteristics at the time of study participation (29.1% vs. 6.9%; $p < 0.001$) and in general (42.1% vs. 19.2%; $p < 0.001$) than participants who indicated no or rare impairment (Table 1).

Furthermore, 406 (88.3%) participants stated that their psoriasis at least rarely prevents them from any leisure activity. When asked which leisure activities were impaired with an open question, 394 participants (97.0%) provided 552 answers. After qualitatively categorizing all given answers, "swimming" (n = 273; 67.2%; e.g., "Swimming in public pools. The chlorine burns the skin."), "sport"

(n = 93; 22.9%; e.g., "I can't go jogging anymore as my knees were destroyed by psoriatic arthritis."), and "stigmatization and appearance" (n = 49; 12.1%; e.g., "Whenever I can't put on anything long enough to hide my disease in public") were the three most mentioned categories (Table 2). Furthermore, many answers indicated a reduction in social contacts. For example, people used expressions such as "meeting new people" and "any activity among people is unpleasant because the strong itching leads to scratching and leaving dandruff everywhere". Many individuals also mentioned abstaining from activities that could exacerbate their symptoms, such as "drinking/eating/partying—all because of the fear of worsening condition following the consumption of unhealthy food/alcohol". Reasons given widely differ within the individuals and the 50 most commonly used words show a multifaceted sense of loss and preoccupation with daily life for participants due to psoriasis (Figure 1).

Table 2. Inductive categories of free-text answers on what leisure activities were avoided due to psoriasis. Quantity, two examples, and respective participant characteristics per category.

Category	Count *n* (%)	Example	Participant (Gender, Age)
Swimming	273 (67.2%)	"Sauna and swimming pool, but only because of the expected looks on the affected areas"	Woman, 32 years
		"Swimming in public pools. The chlorine burns the skin".	Man, 39 years
Sport	93 (22.9%)	"I can't go jogging anymore as my knees were destroyed by psoriatic arthritis".	Man, 32 years
		"Running"	Woman, 51 years
Stigmatization and appearance	49 (12.1%)	"Whenever I can't put on anything long enough to hide my disease in public"	Woman, 50 years
		"Any activity requiring short clothing"	Woman, 21 years
Sauna	32 (7.9%)	"Sauna, bathing"	Man, 73 years
		"Sauna, swimming, nudism"	Woman, 57 years
Sunbathing	30 (7.4%)	"Sunbathing at the lake"	Man, 57 years
		"Sunbathing at the beach"	Man, 30 years
Movements and walking	28 (6.9%)	"Going for a walk"	Woman, 52 years
		"Roughhousing with my son"	Man, 34 years
Going out and meeting friends	26 (6.4%)	"Any activity among people is unpleasant because the strong itching leads to scratching and leaving dandruff everywhere".	Woman, 27 years
		"Visiting restaurants with friends"	Man, 38 years
Other	21 (5.2%)	"Everything you need hands for"	Woman, 67 years
		"Living"	Man, 38 years

3.2. Internet Addiction

Participants reported spending 21.6 ± 12.5 h per week online excluding time at work. About four out of five participants stated being online for private reasons every day (n = 381; 82.8%). Overall, 8.5% (n = 39) of all participants were screened positive for Internet addiction, with no significant difference in gender (female: 8.5% vs. male: 8.7%, p = 0.935), age (<46 years: 9.1 vs. ≥46 years: 8.0%, p = 0.660), and social impairment due to psoriasis ("Never or rarely": 8.5% vs. "Sometimes, frequently, or always": 8.5%, p = 0.997; Figure 2, Table A1).

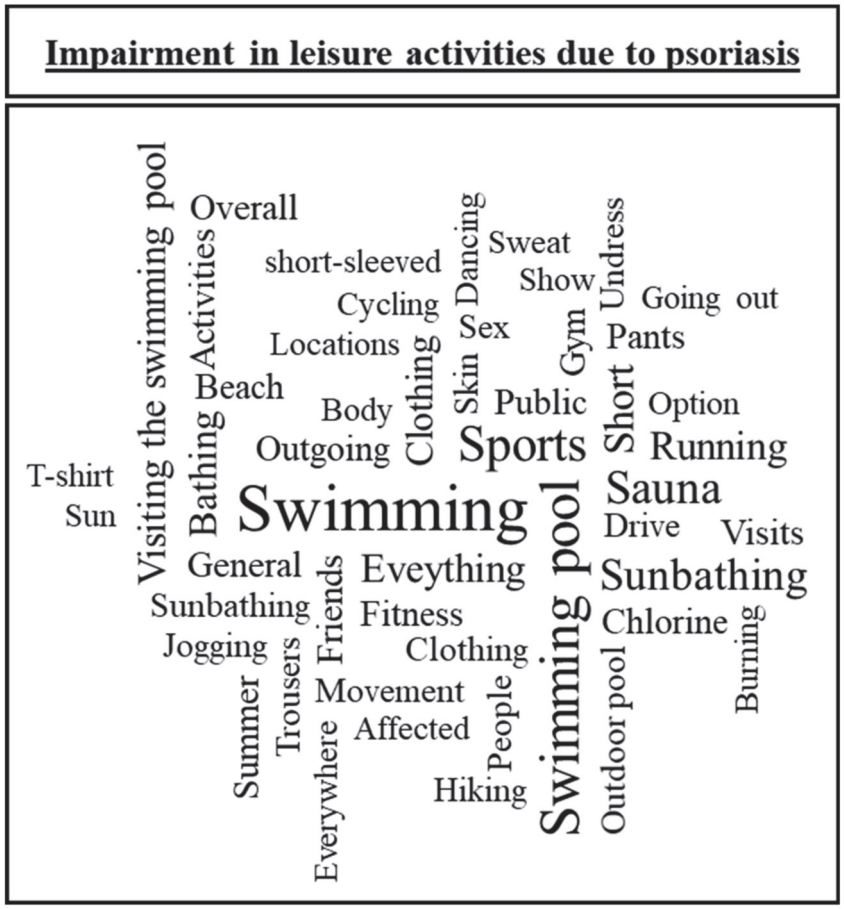

Figure 1. The 50 most common words in free-text answers on the question, which leisure activities were prevented by psoriasis. Words were ranked by frequency. Font size (fs) equals the sweeping break of the third root of word's rank (rx) times maximal font size (fs_{max}) [$fs = fs_{max}*rx^{-1/3}$]. As some words cannot be translated verbatim and free-text answers were given in German, some words are separated in two or more or appear as duplicates.

3.3. Depression, Smoking, and Drinking

Depressive tendencies were found in 40.0% (n = 180) of the participants (Figure 1). Social impairment due to psoriasis (at least "sometimes") was associated with a higher proportion of positive screening results for depression (45.8% vs. 25.2%; $p < 0.001$). Furthermore, 32.6% (n = 150) of all individuals stated to smoke cigarettes daily, and 17.1% (n = 77) were screened positive for alcohol addiction. More women reported a daily smoking habit (38.3% vs. 23.1%; $p = 0.001$; Figure 1), while more men were screened positive for alcohol addiction (25.9% vs. 11.8%; $p < 0.001$). Additionally, younger participants more frequently reported smoking cigarettes daily (41.4% vs. 24.4%; $p < 0.001$). These differences remained significant when controlled in a multiple regression model, resulting in ORs of 2.13 (95% CI: 1.36; 3.34) for women and 0.96 (95% CI: 0.95; 0.98) for age (Table A2).

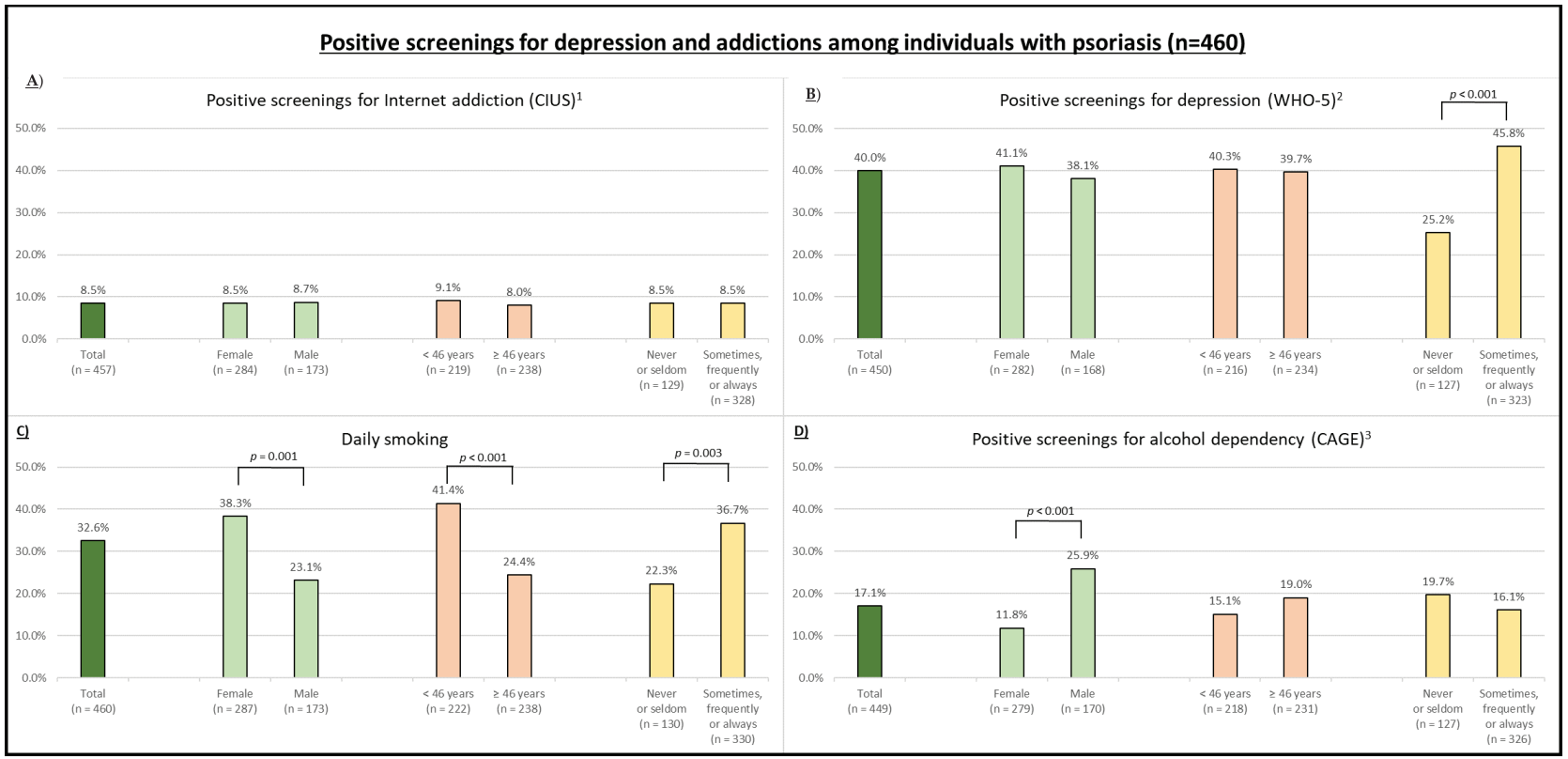

Figure 2. Positive screenings for (**A**) Internet addiction, (**B**) depression, (**C**) cigarette smoking, and (**D**) alcohol dependency. Positive screenings are stratified by gender, age (median split), and social impairment. [1] Measured using the Compulsive Internet Using Scale (CIUS; cutoff: ≥21; range: 0–56). [2] Measured using the World Health Organization (WHO)-Five Well-Being Index (WHO-5) questionnaire (cutoff: ≤29; range: 0–100). [3] Measured using the CAGE questionnaire (cutoff: ≥2; range: 0–4).

4. Discussion

This study aimed to characterize social impairment and estimate the occurrence of Internet addiction along with depression, smoking, and alcohol dependency in individuals with psoriasis recruited via an online, people-centered care approach. Many participants indicated an impairment due to their psoriasis, with swimming and sports being the most commonly mentioned fields of daily life being avoided. Given reasons often focused on stigmatization and pain. Furthermore, a high positive screening rate for Internet addiction and alcohol dependency was found.

4.1. Social Impairment

Overall, 88.3% of participants indicated that their psoriasis prevents them from leisure activities and meeting other people. Thereby, individuals with more social impairment reported higher self-perceived disease severity. This finding is in line with a previous study, which found that individuals with moderate or severe disease severity engaged approximately 30% less in leisure activities than healthy controls did; no difference was observed for participants with little or no disease activity [10]. In our study, we not only found that people avoided specific leisure activities such as swimming and sports but that they also felt stigmatized. This confirms previous findings that stigmatization of skin lesions was associated with social impairment [16]. Most of the participants mentioned avoiding swimming. However, it should be noted that examples for leisure activities such as "Swimming, sauna, sunbathing, ... " were provided as suggestions to give participants ideas for possible answers, potentially resulting in biased free-text answers. The high number of mentions for swimming, however, reflect a problem identified decades ago [41]. In 1989, a study on 104 psoriasis patients found that 72% of patients avoided swimming, 60% avoided sunbathing, and 40% avoided sports. Although sunbathing was also mentioned as an example in this study, it was mentioned less frequently in this sample, while swimming remains an often avoided activity for affected individuals [41]. The stated reasons of shame, stigmatization, and physical sensations such as burning and itching are in line with previous literature [10,41]. The fact that patients still abstain from activities such as swimming because of possible stigmatization emphasizes the importance of current efforts to reduce stigmatization in psoriasis [15,16], which follows the call for action outlined by the WHO [19]. Another point that might be addressed in future research is a possible connection between skin and joint pain as well as itch, and social impairment. Skin pain is an often prevalent symptom [42] and was also frequently reported in the free-text answers.

4.2. Internet Addiction

Positive screening rates for Internet addiction exceeded those reported in the literature [3–5,43]. In comparison to a German representative study among adolescents, this study's results were considerably higher (8.5% vs. 3.2%) [4]. This is surprising, considering the difference in mean age (45.9 years vs. 14.9 years) and tendency for Internet addiction to occur in younger individuals and to decrease with age [3]. Even if we were to consider a higher cutoff value of 28, our detected prevalence of Internet addiction was higher (3.2%) than the prevalence of 1.0% in another German study among 8132 adolescents and adults (mean age: 39.9 years) [3]. Although a third study also used online recruitment via Facebook groups, they only detected a prevalence of 1.2% of Internet addiction in 245 regular Internet users [43]. Lastly, the prevalence of positive screening results also outnumbered the prevalence among 502 psoriasis patients recruited from various dermatological practices and clinics throughout southern Germany (8.5% vs. 3.6%) [5]. Since our results on Internet addiction exceed all previous reported numbers, this could imply that by recruiting participants online and via patient platforms as well as a nationwide physician-lead campaign, we were able to reach a highly vulnerable subgroup of individuals with psoriasis. As another study by Megna et al. found higher signs of inflammation in patients with psoriatic arthritis who practice smartphone overuse [44], future studies should include patient stratification by presence of psoriatic arthritis and differentiation between online

and smart phone addiction. This is, however, one of the first studies to investigate Internet addiction in psoriasis and further investigation should follow.

4.3. Depression, Smoking, and Alcohol Dependency

Our detected value for positive screenings for depression is similar to one of the highest prevalence rates reported by a systematic review on depression in patients with psoriasis (questionnaire-based prevalence: 13.8–39.2%) [17]. The high rate of depression in our study might be explained by the fact that a people-centered care approach was used instead of a patient-centered approach. This could be beneficial in reaching especially vulnerable subgroups of affected individuals. In accordance with preliminary studies in patients with psoriasis [5,18,20,21] and compared to a representative German sample, individuals with psoriasis reported a higher prevalence of daily smoking (32.6% vs. 15.1%) [45] and alcohol dependency (17.1% vs. 3.1%) [45]. The gender distribution for smokers was contrary to that of the general population in which men are more likely to smoke daily than women [45]. Positive screenings for alcohol dependency (17.1%) also exceeded values reported in two recent German studies in patients with psoriasis (8.6–13.5%) [5,18]. Possible explanations might include the anonymous environment of an online survey, a more vulnerable sample in this study, or both.

4.4. Limitations and Strengths

There are some study limitations. As this was an online survey, the truthfulness of participant answers cannot be verified and prevalences were estimated using screening tools, not diagnoses. Additionally, due to the anonymity provided by the online design of this study, social desirability bias could have been reduced. While this is desirable, it makes comparison with previous studies in medical settings more difficult. Selection bias must be taken into account when considering the generalizability of these findings. Mainly individuals receiving information, newsletters, or social media updates from the multiplier institutions were reached. Individuals who are not engaging with online content related to psoriasis, who are participating in other organizations, or who do not have an Internet connection were highly unlikely to participate in our study. However, this might have also led to an especially vulnerable subgroup of affected individuals, which can be desirable when evaluating mental and social impairment. Those with a high disease burden might be more likely to search for further information online and therefore have may have a higher chance of receiving a study invitation through a multiplier organization. Since a high proportion of participants in this study were not currently in medical care, this online-based recruitment strategy allowed us to reach a unique group of individuals, who may not have been considered in traditional clinical trials and registries, further showing the strengths of online outreach. This can broaden the horizon of dermatological research and strengthen people-centered care [29].

5. Conclusions

The study implicates that social impairment and Internet addiction are high among individuals with psoriasis recruited via patient networks in a people-centered care and online approach. Positive screening results for Internet addiction and the other mental health variables exceeded values found for the general population. The findings on social impairment and addictions emphasize the importance of mental burden in psoriasis [19] and, therefore, strengthen evidence on the need for programs to reduce stigmatization [15,16]. Internet addiction was confirmed as an aspect of mental health that should be considered in further research on individuals with psoriasis. Ultimately, the results indicate that inclusion of online self-help platforms and their users in health care research could be a key element in promoting people-centered and not only patient-centered care.

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project administration, M.C.S., B.S., C.L., and A.Z. All authors have read and agreed to the published version of the manuscript.

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Appendix A

Table A1. Differences in positive screenings for depression, daily smoking, alcohol dependency, and Internet addiction when stratified by gender, age (median split), and social impairment.

		Total (n = 460)	Gender		p-Value	Age		p-Value	Psoriasis is Preventing Leisure Activities		p-Value
			Female (n = 287)	Male (n = 173)		<46 years (n = 222)	≥46 years (n = 238)		Never or Rarely (n = 130)	Sometimes, Frequently, or Always (n = 330)	
Internet addiction [3]; n (%)	Yes	39 (8.5%)	24 (8.5%)	15 (8.7%)	0.935	20 (9.1%)	19 (8.0%)	0.660	11 (8.5%)	28 (8.5%)	0.997
	No	418 (91.5%)	260 (91.5%)	158 (91.3%)		199 (90.9%)	219 (92.0%)		118 (91.5%)	300 (91.5%)	
	missing	3	3	0		3	0		1	2	
Depression [1]; n (%)	Yes	180 (40.0%)	116 (41.1%)	64 (38.1%)	0.524	87 (40.3%)	93 (39.7%)	0.908	32 (25.2%)	148 (45.8%)	<0.001
	No	270 (60.0%)	166 (58.9%)	104 (61.9%)		129 (59.7%)	141 (60.3%)		95 (74.8%)	175 (54.2%)	
	missing	10	5	5		6	4		3	7	
Alcohol dependency [2]; n (%)	Yes	77 (17.1%)	33 (11.8%)	44 (25.9%)	<0.001	33 (15.1%)	44 (19.0%)	0.272	25 (19.7%)	52 (16.1%)	0.371
	No	372 (82.9%)	246 (88.2%)	126 (74.1%)		185 (84.9%)	187 (81.0%)		102 (80.3%)	270 (83.9%)	
	missing	11	8	3		4	7		7	4	
Smoking daily; n (%)	Yes	150 (32.6%)	110 (38.3%)	40 (23.1%)	0.001	92 (41.4%)	58 (24.4%)	<0.001	29 (22.3%)	121 (36.7%)	0.003
	No	310 (67.4%)	177 (61.7%)	133 (76.9%)		130 (58.6%)	180 (75.6%)		101 (77.7%)	209 (63.3%)	
	missing	0	0	0		0	0		0	0	

[1] Measured using the Compulsive Internet Using Scale (CIUS; cutoff: ≥21; range: 0–56). [2] Measured using the WHO-Five Well-Being Index (WHO-5) questionnaire (cutoff: ≤29; range: 0–100). [3] Measured using the CAGE questionnaire (cutoff: ≥2; range: 0–4).

Table A2. Associated factors for positive screenings for depression, daily smoking of tobacco as well as alcohol and Internet addiction. Results as crude and adjusted odds ratios.

Dependent Variable	Independent Variables (Reference)	Crude OR (95% CI)	Adjusted OR (95% CI)
Internet addiction [1]	Age	0.98 (0.96–1.01)	-
	Gender (male)	0.97 (0.50–1.91)	-
	Duration of psoriasis	0.97 (0.95–1.00)	0.97 (0.95–1.00)
	Currently in medical care (yes)	0.99 (0.46–2.17)	-
	Severity at the time of study participation (mild)	-	-
	moderate	1.34 (0.56–3.24)	-
	severe	1.29 (0.46–3.60)	-
	Severity in general (mild)	-	-
	moderate	0.54 (0.19–1.53)	-
	severe	0.61 (0.20–1.80)	-
	Social impairment (never or rarely)	1.00 (0.48–2.08)	-
Depression [2]	Age	0.99 (0.98–1.01)	-
	Gender (male)	1.14 (0.77–1.68)	-
	Duration of psoriasis	0.98 (0.97–1.00)	0.98 (0.97–1.00)
	Currently in medical care (yes)	1.32 (0.84–2.09)	-
	Severity at the time of study participation (mild)	-	-
	moderate	1.53 (0.92–2.52)	1.34 (0.80–2.25)
	severe	2.77 (1.55–4.94)	2.13 (1.16–3.91)
	Severity in general (mild)	-	-
	moderate	1.11 (0.53–2.31)	-
	severe	2.08 (0.98–4.43)	-
	Social impairment (never or rarely)	2.51 (1.59–3.96)	2.12 (1.32–3.42)
Daily smoking	Age	0.96 (0.95–0.98)	0.96 (0.95–0.98)
	Gender (male)	2.07 (1.35–3.16)	2.13 (1.36–3.34)
	Duration of psoriasis	0.98 (0.96–0.99)	-
	Currently in medical care (yes)	0.96 (0.60–1.52)	-
	Severity at the time of study participation (mild)	-	-
	moderate	1.36 (0.81–2.26)	-
	severe	1.71 (0.95–3.09)	-
	Severity in general (mild)	-	-
	moderate	2.97 (1.12–7.89)	3.40 (1.24–9.31)
	severe	3.99 (1.48–10.78)	4.58 (1.62–12.96)
	Social impairment (never or rarely)	2.02 (1.26–3.23)	1.77 (1.07–2.94)

Table A2. *Cont.*

Dependent Variable	Independent Variables (Reference)	Crude OR (95% CI)	Adjusted OR (95% CI)
Alcohol dependency [3]	Age	1.01 (0.99–1.03)	-
	Gender (male)	0.34 (0.23–0.63)	0.34 (0.23–0.63)
	Duration of psoriasis	1.01 (1.00–1.03)	-
	Currently in medical care (yes)	1.08 (0.60–1.94)	-
	Severity at the time of study participation (mild)	-	-
	moderate	1.71 (0.88–3.31)	-
	severe	1.10 (0.49–2.48)	-
	Severity in general (mild)	-	-
	moderate	2.76 (0.82–9.37)	-
	severe	1.86 (0.53–6.57)	-
	Social impairment (never or rarely)	0.79 (0.46–1.33)	-

OR = odds ratio; 95% CI = 95% confidence interval; bold values represent significant results at alpha 0.05. [1] Measured using the Compulsive Internet Using Scale (CIUS; cutoff: ≥21; range: 0–56). [2] Measured using the WHO-Five Well-Being Index (WHO-5) questionnaire (cutoff: ≤ 29; range: 0–100). [3] Measured using the CAGE questionnaire (cutoff: ≥ 2; range: 0–4).

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People-centered care for Psoriasis and Urticaria: Are we overlooking Internet Addiction while only considering Patients and Physician settings?

Internet Addiction in skin dieseases

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Abstract

Psoriasis and chronic urticaria (CU) are chronic skin diseases with a high impact on individuals' life and mental health. Some studies indicate a high prevalence of Internet addiction and many affected individuals seem not to utilize health care, but rather search for health-related information online. Aims of the study were to assess Internet addiction as a potential comorbidity in both diseases as well as identify differences in health care utilization between individuals with psoriasis and CU as well as. This cross-sectional study is based on self-reported data from individuals with psoriasis and CU living throughout Germany using the framework of an online survey from 12/2018 to 01/2019. Advertisements on Google and Facebook were used to address Internet users who searched online for information on psoriasis or CU. The study questionnaire comprised questions on demographics, current contact to physicians, disease history as well as validated screening tools for well-being and Internet addiction. Overall, 1,686 participants (74.0% female; 38.5% psoriasis) with a mean age of 36.9 ± 12.9 years were analyzed. Participants with CU were more likely female (89.2% vs. 49.8%; $p<0.001$) and not in medical care compared to participants with psoriasis (60.3% vs. 45.9%; $p<0.001$). Sixteen percent of the participants overall were screened positive for Internet addiction. Furthermore, not utilizing medical care showed a significant association with being screened positive for Internet addiction in participants with CU (adjusted odds ratio (aOR)= 1.49; 95% confidence interval (CI) 1.10-2.02), but not in those with psoriasis. The study revealed a high proportion of affected individuals not being in medical care and a high prevalence of Internet addiction, with individuals with CU not utilizing medical resources having a higher chance of being screened positive for Internet addiction. This underlines the approach of people-centered care and highlights its importance for further research.

Keywords: Chronic skin diseases; Dermatology; Internet addiction; Depression; Mental Health; Epidemiology; People-centered care

Introduction

In Europe, the prevalence of psoriasis ranges between 1.3% and 11.4%, with a reported prevalence of 2.0% in Germany [1,2]. Chronic urticaria (CU) has a point prevalence of 0.5% to 1.0% across Europe [3]. The psychosocial burden of both diseases is high as individuals often experience stigmatization or social and sexual avoidance [4,5] as well as suffer from comorbidities including mental diseases [6,7]. For example, studies demonstrated that psoriasis patients showed an addictive behavior regarding cigarettes and alcohol [8–10]. First studies indicated that psoriasis is potentially associated with other addictive behaviors such as Internet addiction [11,12]. As Internet addiction represents a rapidly rising phenomenon of societies worldwide, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders mentioned it as the most potent problem needing further research. Therefore, it is essential to clarify its presence in people with chronic visible skin diseases, who often withdrawal themselves from social activities [5, 13, 14]. However, those studies used heterogeneous settings as one study included patients recruited by dermatologists and the other people recruited via psoriasis self-help groups and showed a wide variation in the Internet addiction rate. The association between CU and Internet addiction has not been investigated so far.

Adequate treatment can not only improve patients' symptoms, but may also reduce mental health burden [15,16]. However, there are barriers in the use of modern treatments and not every patient receives therapy according to the respective national guidelines [17, 18]. Furthermore, it is important to distinguish between patients and affected individuals as some persons do not contact a physician due to their skin disease [19, 20]. The World Health Organization (WHO) hence demands an improvement of people-centered care in order to bridge the gap between physicians and affected individuals [21, 22]. Accordingly, psoriasis should be considered as model disease and according to the WHO other chronic skin diseases were to be included if possible [21].

When reaching out for individuals suffering from their disease, but do not consult a doctor, prior research showed that usage of the Internet might be beneficial [23, 24] as it is a commonly used source for health information [25]. One study showed that 80% of affected people used the Internet to receive initial or additional information about their disease [26]. Additionally, online search analysis demonstrated that the burden of specific diseases is high and anonymous online settings might reduce social desirability

77 bias [27]. Reaching out for affected individuals online showed first good results in the field of
78 dermatology [28].
79 The aims of this study were (I) to estimate the prevalence of Internet addiction in people suffering from
80 psoriasis and CU reached online and (II) to identify differences in health care utilization between
81 individuals with both diseases.

82 **Methods**

83 *Study design and participants*

84 This non-interventional cross-sectional study assessed self-reported data from individuals with psoriasis
85 and CU living throughout Germany using the framework of an online survey from December 2018 to
86 January 2019. Recruitment was carried out through online banner advertisement on Facebook and
87 Google. The banners stated e.g. "Psoriasis Survey - participate now!" or "Urticaria – looking for
88 participants in a survey," and specifically addressed individuals whose prior search behavior indicated
89 interest in these diseases and therefore represent a certain sub-population of individuals with the
90 respective disease. Before starting the survey, participants gave their electronic informed consent.
91 Inclusion criteria were (I) 18 years and older, (II) self-stated physician diagnosis of psoriasis or CU and
92 associated symptoms within the last three months, and (III) self-stated ability to complete the German
93 questionnaire. All these criteria had to be answered before being able to start with the questionnaire. If
94 one question was neglected, participants were guided to the respective self-help web-pages. To ensure
95 data quality, participants answering less than 80% of study questionnaire were excluded. Ethical
96 clearance for all analyses was sought from the Ethics Commission of the Faculty of Medicine of the
97 Technical University of Munich.

98 *Questionnaire*

99 The study was designed by a consortium of two experienced dermatologists and two epidemiologists
100 and variables were only added or deleted after consensus. Questions asked for general demographics
101 (age, gender, relationship status, current employment), current utilization of health care system, disease
102 history (duration of disease, time span from first symptoms to first diagnoses), and mental health aspects
103 including a short version of the patient health questionnaire (PHQ-D) [29] as well as the short version
104 of the Compulsive Internet Using Scale (CIUS) [30]. The PHQ-D is a screening tool for depression and

consists out of two dichotomous questions ('During the past month, …': '(I) have you often been bothered by feeling down, depressed, or hopeless?' or '(II) have you often been bothered by little interest or pleasure in doing things?') [29]. The score ranges from 0 to 2 and a score of ≥1 is considered as a positive screening for further investigation towards depression. The CIUS is a screening tool for Internet addiction and consists of five questions using a five-point Likert scale ranging from 'never' (0) to 'very often' (4). It represents a reliable questionnaire (Cronbach's alpha: 0.77) and the suggested cut-off value is ≥7 for a positive screening result, resulting in a sensitivity of 0.95 and a specificity of 0.87 [30, 31]. To minimize false positive results and to increase reliability of prevalence estimations of Internet addiction, the cut-off value for the estimation of prevalence was increased to ≥9, whereby the specificity increases to 0.96 [30]. Additionally, time spent online per day for leisure as well as days per week spent online (both not including activities for work) were inquired and summarized as hours spent online per week for further analyses. Disease severity was measured asking for participants self-stated affected body surface area (BSA), which was to be estimated in hands (one hand = 1% of body surface) [32]. A value of ≥10 indicated a moderate to severe form of psoriasis. Disease control of CU was measured using the 'Urticaria Control Test' (UCT), which consists of four questions being answered using a five-point Likert scale (range 0-16). It refers to participants' disease during the last four weeks and a cut-off of ≤11 indicates a poorly controlled CU [33]. To assure high quality of data and minimize bias due to missing data, several plausibility checks were implemented before the analysis (e.g. the time since diagnosis or onset of symptoms could not be higher than the age).

Statistics and data management

Descriptive data were generated. Data were stratified by disease as well as by utilization of medical care. Linear variables were compared using unpaired t-test and categorical variables were compared using Pearson's chi-squared test. To identify factors associated with compulsive Internet use, a logistic regression was carried out, yielding the screening with literature recommended CIUS cut-off value (≥7) as dependent variables. As independent variables, all reported variables available for psoriasis and CU were added (age, gender, disease (psoriasis/CU), disease duration, disease duration before consulting a physician for the first time, utilization of health care system, PHQ-D, relationship status). Furthermore, two disease specific models were calculated including BSA and UCT, respectively. All crude odds ratios

(OR) and 95% confidence intervals (CI) were calculated. To visualize multicollinearity, correlations were calculated and reported using the Spearman's rank correlation coefficient. To minimize it, all variables were added in a multiple regression model and selected via backward selection. After elimination, adjusted ORs (aOR) and respective 95% CIs were calculated. IBM SPSS Statistics (Version 25, IBM Corporation, Armonk, NY, USA) was used for all analyses and alpha was set to 0.05.

Results

Participants' characteristics and comparison of disease

Overall, 3,222 individuals opened the first page of the survey and 1,686 completed it, resulting in a rate of 50.8% (Fig. 1). Of the included 1,686 participants, 74.0% were females and the participants' mean age was 36.9 ± 12.9 years. More participants with CU took part (n_{cu}=1,037 vs. n_{pso}=649) and those had a higher proportion of females (89.2% vs. 49.8%, p<0.001) as well as a younger mean age (33.4 ± 10.9 years vs. 42.5 ± 13.7 years; p<0.001). Mean UCT was 7.9 ± 3.9, indicating that 79.6% of participants with CU were uncontrolled. Mean BSA was 6.1 ± 8.0, with a mild disease in 83.6% of participants with psoriasis. Individuals with psoriasis indicated a longer disease duration (18.1 ± 12.7 years vs. 10.0 ± 9.3 years, p<0.001) and a longer timespan between the first symptoms and consulting a physician (7.0 ± 7.9 years vs. 3.6 ± 5.4 years; p<0.001). Around 70% of participants in both groups scored ≥1 on the PHQ-D, which indicates a psychosocial disturbance, and about one in two participants scored two, which indicates further investigation for the presence of a depressive tendency.

Estimated prevalence of Internet addiction

In the CU group, people not being in medical care had significantly higher CIUS score (5.0 ± 3.8 vs. 4.2 ± 3.6; p=0.001) and a higher proportion of positive screenings for compulsive Internet use (cut-off: ≥7) than those receiving medical care (29.4% vs 22.6%; p=0.014; Table 2). In the psoriasis group, no difference was observed (Table 2). Participants not consulting a physician reported a longer time spent online within a week (21.4 ± 20.2 h/week vs. 19.9 ± 18.8 h/week; p=0.130).

Overall, 16.0% of participants were screened positive for compulsive Internet use (cut-off: ≥ 9) indicating an Internet addiction. The proportion of positive screenings was not significantly higher among participants not receiving medical care (17.6% vs. 14.2%; p=0.058) and participants with CU (16.9% vs. 14.6%; p=0.223; Fig. 2).

Associated factors for Internet addiction

Of all participants, 1,618 (96.0%) had complete datasets and were included in the first logistic regression model. The chance of having a positive screening for Internet addiction decreased with rising age (aOR=0.97; 95% CI 0.96-0.98; Table S1). Compared to that, being not in medical care (aOR=1.30; 95% CI 1.03-1.63), not being in a relationship (aOR=1.32; 95% CI 1.02-1.70), and having higher scores in the PHQ-D were associated with a positive screening for Internet addiction ($aOR_{PHQ\text{-}D=1}$=1.51; 95% CI 1.06-2.14; $aOR_{PHQ\text{-}D=2}$=2.35 95% CI 1.78-3.11; Fig. 3).

When stratified by disease, the association of gender vanished in both diseases. The high correlation coefficient of gender and disease (r_s=0.44; p<0.001; Table S2) therefore indicated an effect modifying nature of gender in this model. Furthermore, the association of medical care and compulsive Internet use vanished in participants with psoriasis, while the aOR increased in CU (aOR=1.49; 95% CI 1.10-2.02).

Stratification by the utilization of medical care

The proportion of people currently not in medical care was significantly higher among individuals suffering from CU than psoriasis (60.3% vs. 45.9%; p<0.001; Table 1). In general, participants currently receiving medical care were younger (35.6 ± 12.5 years vs. 38.5 ± 13.2; p<0.001) and had waited longer after onset of symptoms until they consulted a physician (6.4 ± 7.7 years vs. 4.8 ± 6.6 years; p<0.001). They showed a longer disease duration (13.6 ± 11.3 years vs. 12.3 ± 11.5 years; p=0.026) compared to individuals who reported not receiving medical care. Patients with CU in medical care showed a lower UCT (6.9 ± 3.9 vs. 8.5 ± 3.8; p<0.001), indicating that they had a less controlled disease. Additionally, participants with CU not seeking medical care showed an increased CIUS score (5.0 ± 3.8 vs. 4.2 ± 3.6; p<0.001) and more positive screenings for compulsive Internet use (29.4% vs. 22.6%; p=0.014) compared to those who were in medical care. Participants with psoriasis showed the same trend, however it was not significant. Furthermore, PHQ-D was more likely to be higher in participants seeing a physician for their CU, while no significant difference was identified within participants with psoriasis (Table 2).

Discussion

The aims of this study were to (I) estimate the prevalence of Internet addiction among people with psoriasis and CU reached online and (II) to identify differences in health care utilization between both

diseases. By using online advertisement, a high proportion of individuals who were currently not in medical care was reached. Positive screening rate for Internet addiction was high and the chance to have a positive screening was higher in younger participants, in individuals who were currently not seeing a doctor, and in individuals having depressive tendencies.

Stratification by disease

Although it is reported that females have a slightly higher prevalence for CU than men [3,34], the proportion of females with reported CU in this study was very high. One possible explanation might be the higher frequency of young individuals and women searching for health related information online [33-35]. However, this assumption is not supported by age and gender distribution compared to individuals with psoriasis participating in the survey. Yet, it remains unclear why these gender differences were reached and needs future research.

Estimated prevalence of Internet addiction

Reported values of Internet addiction in Germany among the general population range from 1.0 to 5.0%, depending on age group [38, 39]. In 2014, a large German study including 8,130 individuals reported an Internet addiction prevalence of 1.0 to 1.5% [40]. Accordingly, the herein found rate for positive screening of 16.0% appears to be tremendously high. One important reason for these considerable differences could be that participants showing symptoms of an Internet addiction are more likely to spend more time online and therefore being reached via an online survey or online advertisements. As this study online included people reached online, individuals with no access to the Internet were not able to participate in this study. However, a comparable study reported a prevalence of 1.2% among 249 regular Internet users. The authors also relied on a web-based design using Facebook for recruitment and the study period lasted less than two months [39]. The study results, however, did not only indicate a higher rate of Internet addiction in comparison to the general population, but also in comparison with two previous studies among people with psoriasis. For example, in a study among individuals with psoriasis reached via online self-help groups the reported prevalence was 8.5% [12] and in a study among psoriasis patients recruited offline, in clinics and dermatological offices, the prevalence was 3.8% [11]. Therefore, the way affected individuals are reached seems to be essential for the frequency of positive screenings for Internet addiction. Although using an online setting to investigate Internet addiction might overestimate the actual problem, this might not be the only reason for these large

differences, but also promotes the use of online tools and advertisements to reach a potentially vulnerable sub-sample of people with chronic skin diseases. While there is no evidence on rate of Internet addiction among people with CU in the literature so far, a previous study indicated compulsive tendencies in patients with urticaria [41]. This is an important finding and needs further investigation.

Associated factors for Internet addiction

Like in the literature, Internet addiction was associated with younger age [39] and showed no gender differences [40]. Additionally, the study could confirm depressive tendency being positively associated with Internet addiction [42, 43]. As this is the first study which investigate the issue in chronic skin disease including individuals with and without contact to a physician, it is highly interesting that affected individuals who were currently not in medical care had a higher chance of a positive screening for Internet addiction. When stratified by disease, this difference vanished in participants with psoriasis, while it increased in participants with CU. In combination with diminishing effects of relationship status due to stratification, this indicated the role of disease as possible confounder. Therefore, the exact nature of this association and potential causality should be investigated in future studies. Further studies are needed and registry data or data including a suitable control group might be highly beneficial.

Stratification by the utilization of medical care

The study indicated that people being not in medical care had a milder disease form which might be due to the fact that their disease might be already controlled compared to those who are receiving medical care. The mean UCT value of 8.5 was remarkably below the score indicating a controlled disease (=12). Indeed, three out of four people not being in medical care indicated an uncontrolled CU. However, controlling the disease was reported to be a major aim in CU [34, 44, 45] and the proportions of poorly controlled individuals was higher in this study than previously reported in the literature (79.6% vs. 36.5%) [34]. A possible explanation might be that individuals with a less controlled CU are more likely to be bothered and therefore search for information online. Subsequently, the study's specific advertisements might mainly have reached these individuals. By all means, modern and effective therapies do not have an added value if people do not receive them [46].

The longer disease duration of participants of both groups not being in medical care underlines the necessity of medical advice and care. Furthermore, it could indicate a drop out of medical care as a result of long disease duration and frustrated expectations in sufficient and promising treatments. This would

be in accordance with previous findings [47].

Participants with CU receiving medical care reported depressive tendencies more often. While about one in three participants not seeing a physician showed no signs of depressive tendency, in the sub-group of participants currently under medical care only one in five did. An explanation for this difference might be the high proportion of poorly controlled CU in the first group, which is reported to be highly burdening [48]. Furthermore, physicians, especially dermatologists could be sensitized to this issue.

Limitations and strengths

There are some study limitations. First of all, study participants stated self-reported that they suffer either from psoriasis or CU and study fraud cannot be excluded. Measures to minimize the chance of including bots and fraudsters were taken in accordance with existing literature (no “back” button, plausibility checks) [49]. However, due to the anonymous study design measures including geolocation or the IP-address of participants were not feasible, even though they were shown to be highly effective [49, 50]. Furthermore, all answers were self-stated and so, for example, BSA in participants with psoriasis might differ from actual BSA measured by a dermatologist. Another limitation is that no exact response rate can be stated. It is known, that 50.8% of individuals who reacted via the advertisement took part in the survey, however it is unclear for how many Internet users the survey was displayed. Additionally, there was a large potential of selection bias. The proportion of female participants was extremely high, although there are no considerable differences in the prevalence of psoriasis and CU among females and males. Furthermore, only individuals with Internet access and only those actively searching for psoriasis or CU related topics have been reached. This substantially reduces the chance of achieving a representative sample of all individuals with psoriasis and CU, respectively. However, this might also be a major strength of this study: participants might not be representative for all individuals with psoriasis or CU, but it highlights the need to reach affected individuals. Those individuals suffering from the symptoms of their disease might be more likely to search online and subsequently react to the advertised posts. Furthermore, more than half of all participants were not in medical care and therefore are highly unlikely to be reached throughout conservative epidemiological studies and registries focusing on patients instead of all affected people. Consequently, this approach might contribute to broaden the horizon of medical research and could be promising to address individuals with high disease

burden and no contact to a physician, underlining its importance mentioned in a prior review [28].

Conclusion

In conclusion, many individuals with psoriasis and CU were reached through this online survey, of those a large proportion reported to receive no medical care. The study revealed a high occurrence of Internet addiction in participants, demonstrating that individuals with CU not being in medical care have a higher chance of being screened positive. Accordingly, these findings underline the importance of a people-centered approach and the potential of online settings for dermatological research [28]. Additionally, it reveals that online surveys might be a valuable tool if vulnerable groups have to be included in future research. Future studies could include an age and gender adjusted control group as well as health insurance data to clarify whether the risk of Internet addiction is increased among patients with psoriasis or CU. They should focus on identifying ways to reach individuals not seeking medical care despite suffering from these diseases.

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Conflict of Interest

MCS received personal fees from Novartis Pharma GmbH. LT received unrestricted research grants and personal fees from Novartis Pharma GmbH. NW acted as advisor, received lecture honoraria and participated in clinical trials/studies of Novartis Pharma GmbH. AZ acted advisor, received lecture honoraria, received unrestricted research grants and participated in clinical trials/studies of Novartis Pharma GmbH. DB, EH and NW are employees of Novartis Pharma GmbH

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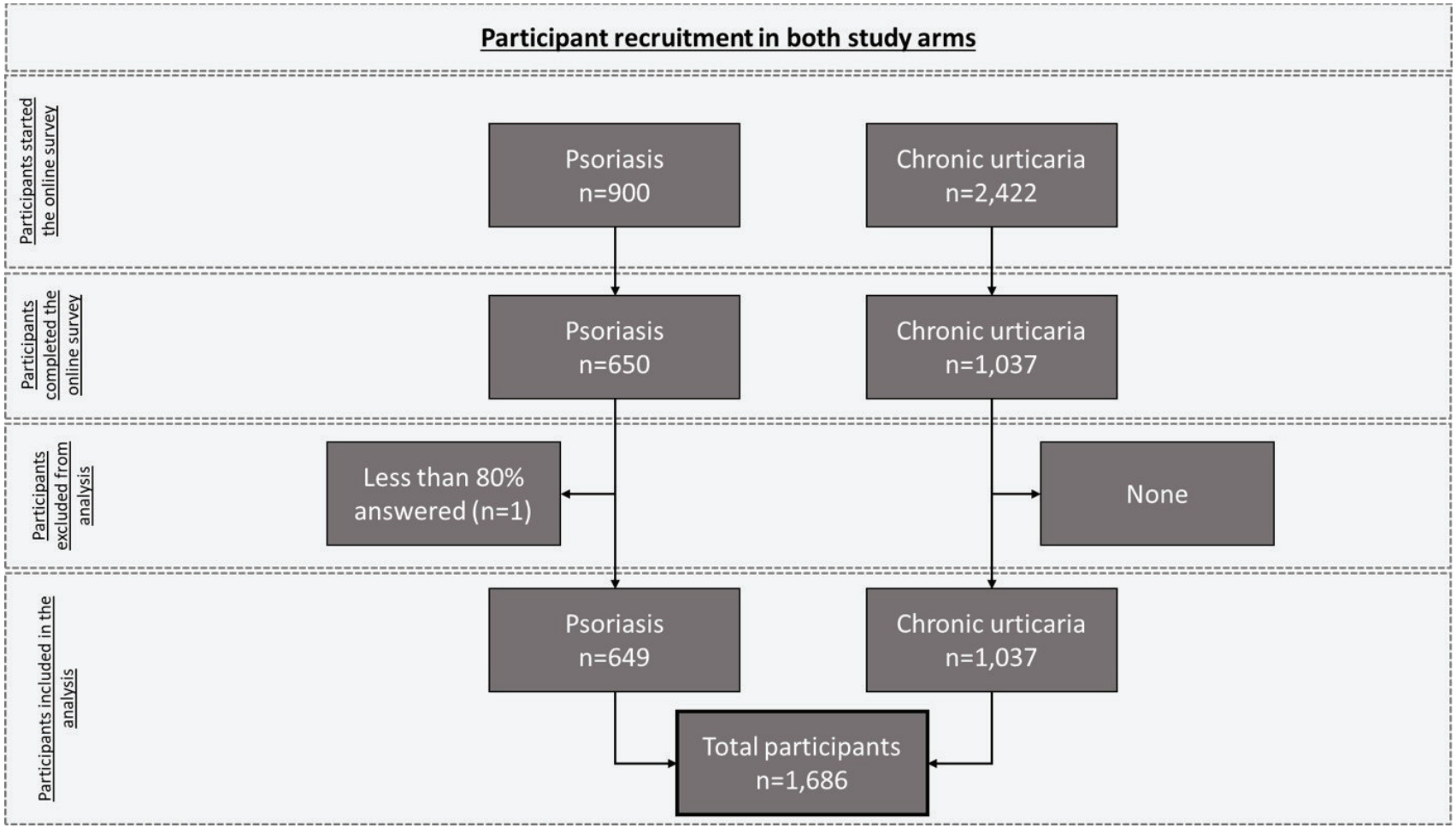
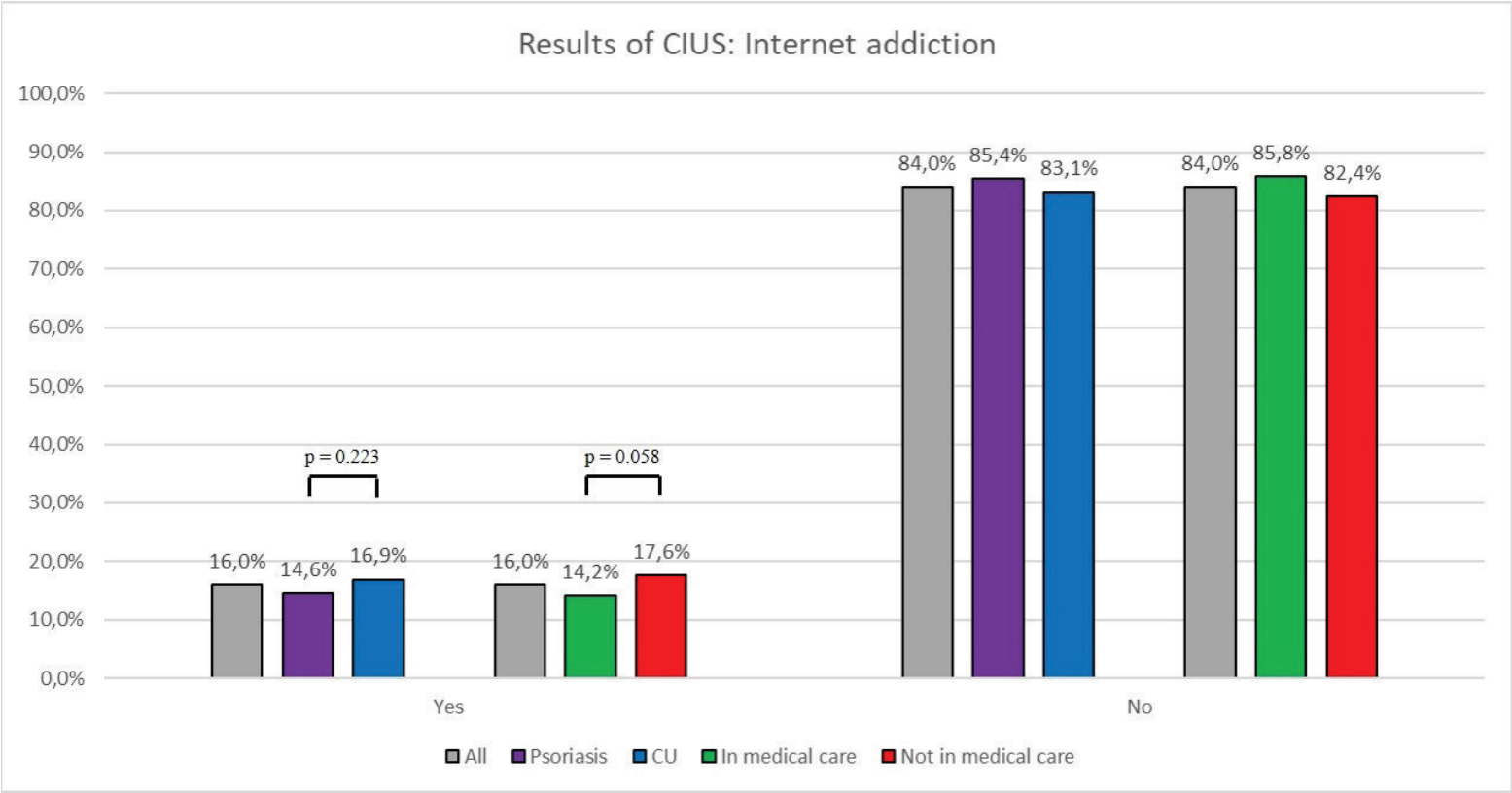
Legends for Figures

Figure 1: Flow chart of participant recruitment and exclusions in both study arms.

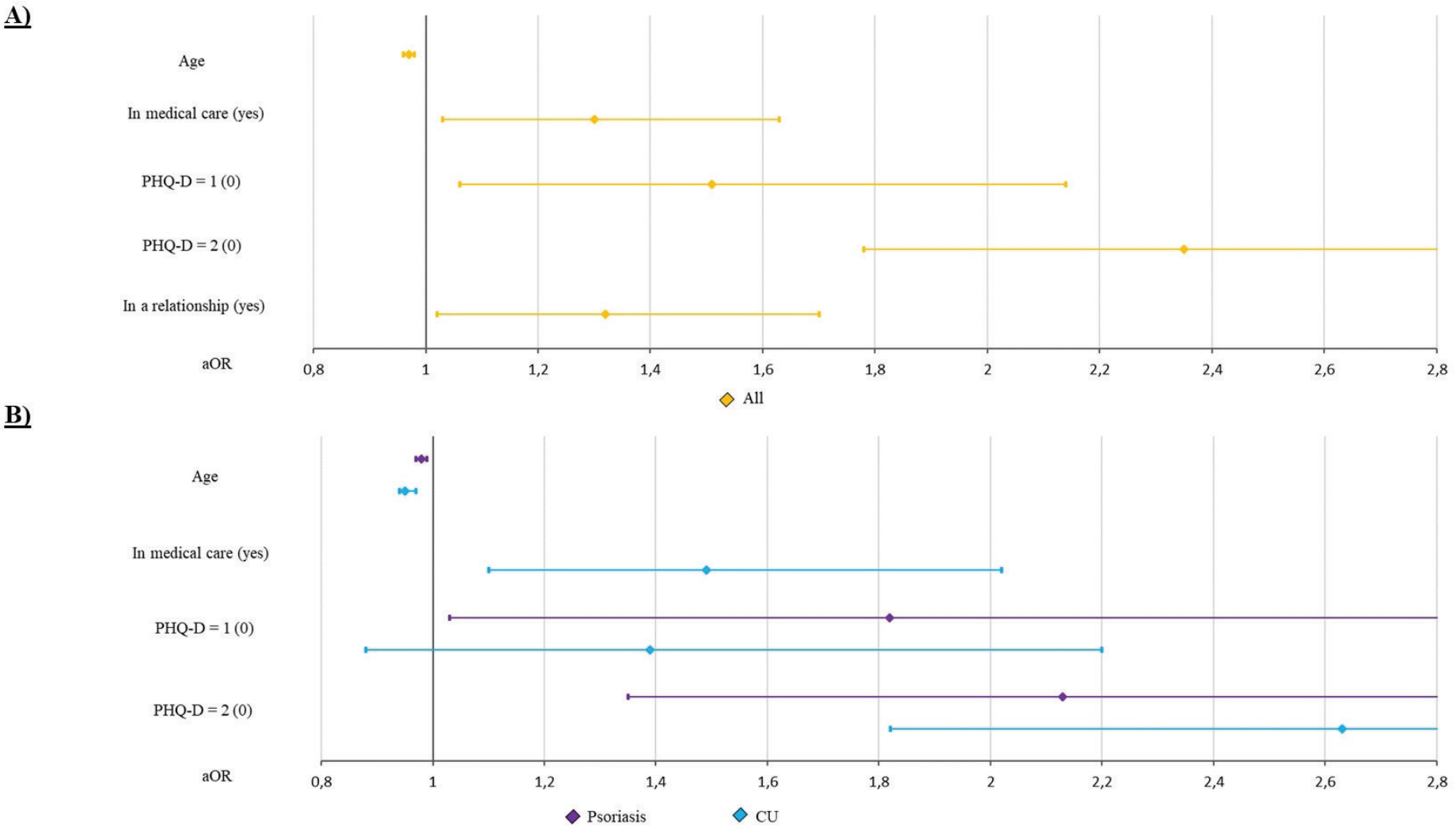
Figure 2: Prevalence of positive screenings for Internet addiction (results of the short form of the Compulsive Internet Using Scale; cut-off ≥9) stratified by disease and utilization of medical care. CU = chronic urticarial; CIUS=short form of the Compulsive Internet Using Scale.

Figure 3: Results of the multiple regression that showed associated factors with the positive screening on compulsive Internet use. A) including all participants; B) Stratified by disease. aOR = adjusted odds ratio; Age in years; PHQ-D = short version of the patient health questionnaire.


Participant recruitment in both study arms
Participants started the online survey
Psoriasis n=900
Chronic urticaria n=2,422
Participants completed the online survey
Psoriasis n=650
Chronic urticaria n=1,037
Participants excluded from analysis
Less than 80% answered (n=1)
None
Participants included in the analysis
Psoriasis n=649
Chronic urticaria n=1,037
Total participants n=1,686


Results of CIUS: Internet addiction
100,0%
90,0%
80,0%
70,0%
60,0%
50,0%
40,0%
30,0%
20,0%
10,0%
0,0%
p = 0.223
p = 0.058
16,0%
14,6%
16,9%
16,0%
14,2%
17,6%
84,0%
85,4%
83,1%
84,0%
85,8%
82,4%
Yes
No
All
Psoriasis
CU
In medical care
Not in medical care

Factors associated with compulsive Internet use in an adjusted model for A) all participants and B) participants stratified by disease



Tables

Table 1: General characteristics of study population stratified by disease.

			Total (n=1,686)	Participants stratified by disease		P-value
				Psoriasis (n=649)	Chronic Urticaria (n=1,037)	
Age [Mean ± SD]			36.9±12.9	42.5±13.7	33.4±10.9	<0.001
Gender [n (%)]		female	1248 (74.0)	323 (49.8)	925 (89.2)	<0.001
		male	438 (26.0)	326 (50.2)	112 (10.8)	
BSA	[Mean ± SD]		NA	6.1±8.0	NA	NA
	[n (%)]	mild	NA	539 (83.6)	NA	
		moderate / severe	NA	106 (16.4)	NA	
		missing	NA	4	NA	
UCT	[Mean ± SD]		NA	NA	7.9±3.9	
	[n (%)]	controlled	NA	NA	212 (20.4)	
		Poorly controlled	NA	NA	825 (79.6)	
Disease duration	[Mean ± SD; years]		13.0±11.4	18.1±12.7	10.0±9.3	<0.001
	[n (%)]	≤ 10 years	871 (53.8)	216 (35.3)	655 (65.1)	<0.001
		> 10 years	747 (46.2)	396 (64.7)	351 (34.9)	
Disease duration before consulting a physician [Mean ± SD; years]			5.7±7.3	3.6±5.4	7.0±7.9	<0.001
Currently in medical care [n (%)]		Yes	763 (45.3)	351 (54.1)	412 (39.7)	<0.001
		No	923 (54.7)	298 (45.9)	625 (60.3)	
Profession [n (%)]		full-time	812 (48.2)	348 (53.6)	464 (44.7)	<0.001
		part-time	322 (19.1)	91 (14.0)	231 (22.3)	
		other	472 (28.0)	174 (26.8)	298 (28.7)	
		unemployed	80 (4.7)	36 (5.5)	44 (4.2)	
PHQ-D-Score [n (%)]		0	503 (29.8)	213 (32.8)	290 (28.0)	0.087
		1	333 (19.8)	118 (18.2)	215 (20.7)	
		2	850 (50.4)	318 (49.0)	532 (51.3)	
In a relationship [n (%)]		Yes	1,273 (75.5)	485 (74.7)	788 (76.0)	0.559
		No	413 (24.5)	164 (25.3)	249 (24.0)	
CIUS Score [Mean ± SD]			4.6±3.6	4.4±3.5	4.7±3.7	0.157
Compulsive Internet use [n (%)]		Yes	431 (25.6)	154 (23.7)	277 (26.7)	0.172
		No	1255 (74.4)	495 (76.3)	760 (73.3)	

Differences were compared using unpaired t-test and Chi square test. SD=Standard deviation; NA=Not applicable; BSA=Body surface area (self-stated); UCT=Urticaria Control Test; PHQ-D= short version of the patient health questionnaire; CIUS=short form of the Compulsive Internet Using Scale. Significant results printed bold.

Table 2: General characteristics of participants stratified by utilization of health care system and disease.

		Total (n=1,686)		P-value	**Psoriasis (n=649)**		P-value	**Chronic Urticaria (n=1,037)**		P-value
		In medical care (n=763)	**Not in medical care (n=923)**		**In medical care (n=351)**	**Not in medical care (n=298)**		**In medical care (n=412)**	**Not in medical care (n=625)**	
Age [Mean ± SD]		38.5±13.2	35.6±12.5	**<0.001**	43.7±13.7	41.0±13.7	**0.013**	34.0±10.9	33.0±10.9	0.159
Sex [n (%)]	Female	539 (70.6)	709 (76.8)	**0.004**	172 (49.0)	151 (50.7)	0.672	367 (89.1)	558 (89.3)	0.918
	Male	224 (29.4)	214 (23.2)		179 (51.0)	147 (49.3)		45 (10.9)	67 (10.7)	
BSA [Mean ± SD]		6.4±8.0	5.7±8.1	0.261	6.4±8.0	5.7±8.1	0.261	NA	NA	NA
UCT [Mean ± SD]		6.9±3.9	8.5±3.8	**<0.001**	NA	NA	NA	6.9±3.9	8.5±3.8	**<0.001**
Disease duration [Mean ± SD; years]		12.3±11.5	13.6±11.3	**0.026**	16.9±12.7	19.5±12.6	**0.014**	8.5±8.7	10.9±9.5	**<0.001**
Disease duration before consulting a physician [Mean ± SD; years]		4.8±6.6	6.4±7.7	**<0.001**	3.5±5.3	3.7±5.6	0.669	5.9±7.3	7.7±8.2	**<0.001**
PHQ-D-Score [n (%)]	0	199 (26.1)	304 (32.9)	**0.008**	112 (31.9)	101 (33.9)	0.764	87 (21.1)	203 (32.5)	**<0.001**
	1	163 (21.4)	170 (18.4)		67 (19.1)	51 (17.1)		96 (23.3)	119 (19.0)	
	2	401 (52.6)	499 (48.6)		172 (49.0)	146 (49.0)		229 (55.6)	303 (48.5)	
Hours per week spent on the Internet for leisure[Mean ± SD]		19.9±18.8	21.4±20.2	0.130	19.3±18.8	22.1±21.7	0.077	20.5±18.7	21.1±19.4	0.654
CIUS Score [Mean ± SD]		4.3±3.5	4.8±3.7	**<0.001**	4.3±3.5	4.5±3.6	0.444	4.2±3.6	5.0±3.8	**0.001**
Compulsive Internet use [n (%)]	Yes	172 (22.5)	259 (28.1)	**0.010**	79 (22.5)	75 (25.2)	0.427	93 (22.6)	184 (29.4)	**0.014**
	No	591 (77.5)	664 (71.9)		272 (77.5)	223 (74.8)		319 (77.4)	441 (70.6)	

Differences were compared using unpaired t-test and Chi square test. SD=Standard deviation; NA=Not applicable; BSA=Body surface area (self-stated); UCT=Urticaria Control Test; PHQ-D=short version of the patient health questionnaire; CIUS=short form of the Compulsive Internet Using Scale; Significant results printed bold

Supplementary Tables

Table S1: Associated factors with the occurrence of Internet addiction in individual logistic regressions and in a multiple logistic regression model for all participants and stratified by disease.

Dependent variable	Independent variables (reference)		Crude OR (95% CI)	Adjusted OR (95% CI)
Internet addiction (CIUS cut-off: ≥7) *n = 1618*	Age [years]		**0.97 (0.96-0.98)**	**0.97 (0.96-0.98)**
	Gender (female)		1.05 (0.82-1.35)	-
	Disease (psoriasis)		1.17 (0.93-1.47)	-
	Disease duration [years]		0.99 (0.99-1.00)	-
	Disease before consulting a physician [years]		1.01 (0.99-1.02)	-
	In medical care (yes)		**1.34 (1.07-1.67)**	**1.30 (1.03-1.63)**
	PHQ-D (0)	1	**1.57 (1.11-2.22)**	**1.51 (1.06-2.14)**
		2	**2.34 (1.78-3.09)**	**2.35 (1.78-3.11)**
	In a relationship (yes)		**1.42 (1.11-1.81)**	**1.32 (1.02-1.70)**
Internet addiction (CIUS cut-off: ≥7; psoriasis) *n = 609*	Age [years]		**0.98 (0.97-0.99)**	**0.98 (0.97-0.99)**
	Gender (female)		1.06 (0.74-1.52)	**-**
	BSA		1.01 (0.99-1.04)	**-**
	Disease duration [years]		1.00 (0.98-1.01)	-
	Disease before consulting a physician [years]		1.02 (0.99-1.06)	-
	In medical care (yes)		1.16 (0.81-1.66)	-
	PHQ-D (0)	1	**1.86 (1.07-3.24)**	**1.82 (1.03-3.23)**
		2	**2.19 (1.40-3.41)**	**2.13 (1.35-3.38)**
	In a relationship (yes)		1.30 (0.87-1.95)	**-**
Internet addiction (CIUS cut-off: ≥7; CU) *n = 1,006*	Age [years]		**0.95 (0.94-0.97)**	**0.95 (0.94-0.97)**
	Gender (female)		1.34 (0.88-2.05)	-
	UCT-score		0.98 (0.94-1.01)	-
	Disease duration [years]		1.00 (0.98-1.01)	-
	Disease before consulting a physician [years]		1.00 (0.98-1.02)	-
	In medical care (yes)		**1.43 (1.07-1.91)**	**1.49 (1.10-2.02)**
	PHQ-D (0)	1	1.42 (0.91-2.20)	1.39 (0.88-2.20)
		2	**2.41 (1.69-3.44)**	**2.63 (1.82-3.80)**
	In a relationship (yes)		**1.49 (1.10-2.04)**	**-**

OR = odds ratio; CIUS = short version of the Compulsive Internet Using Scale; PHQ-D = short version of the patient health questionnaire; CU = chronic urticaria; BSA=Body surface area (self-stated); UCT=Urticaria Control Test. Significant results printed bold.

Table S2: Spearman correlations for variables entered in the multiple regression model.

		Age [years]	Gender (female)	Disease (psoriasis)	Disease duration [years]	Disease before consulting a physician [years]	In medical care (yes)	PHQ-D	In a relationship (no)
Age [years]	r_s	1.000	**0.173**	**-0.328**	**0.323**	0.013	**0.112**	-0.017	**0.050**
	p-value	.	**<0.001**	**<0.001**	**<0.001**	0.596	**<0.001**	0.475	**0.040**
Gender (female)	r_s		1.000	**-0.438**	**0.134**	**-0.164**	**0.070**	**-0.086**	**-0.059**
	p-value		.	**<0.001**	**<0.001**	**<0.001**	**0.004**	**<0.001**	**0.016**
Disease (psoriasis)	r_s			1.000	**-0.351**	**0.318**	**-0.140**	0.037	0.014
	p-value			.	**<0.001**	**<0.001**	**<0.001**	0.128	0.559
Disease duration [years]	r_s				1.000	**0.461**	**-0.084**	**-0.068**	-0.011
	p-value				.	**<0.001**	**0.001**	**0.006**	0.669
Disease before consulting a physician [years]	r_s					1.000	**-0.144**	-0.017	0.011
	p-value					.	**<0.001**	0.494	0.661
In medical care (yes)	r_s						1.000	**0.058**	0.022
	p-value						.	**0.017**	0.369
PHQ-D	r_s							1.000	**-0.060**
	p-value							.	**0.014**
In a relationship (yes)	r_s								1.000
	p-value								.

CIUS = short version of the Compulsive Internet Using Scale; PHQ-D = short version of the patient health questionnaire; Significant results printed bold.

Von:	JDE Editorial Office
An:	Schielein, Maximilian; Tizek, Linda; daniel.baeumer@novartis.com; elena.hillmann@novartis.com; katrin.romer@novartis.com; Nicola.Wagner@uk-erlangen.de; Zink, Alexander
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Datum:	Sonntag, 6. Dezember 2020 19:17:39

06-Dec-2020

Dear Mr. Schielein:

It is a pleasure to accept your manuscript entitled "People-centered care for Psoriasis and Urticaria: Are we overlooking Internet Addiction while only considering Patients and Physician settings?" in its current form for publication in The Journal of Dermatology. The comments of the reviewer(s) who reviewed your manuscript are included at the foot of this letter.

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Thank you for your fine contribution. On behalf of the Editors of The Journal of Dermatology, we look forward to your continued contributions to the Journal.

Sincerely,
Prof. Masutaka Furue
Editor in Chief, The Journal of Dermatology
E-mail: jd@dermatol.or.jp

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Editor-in-Chief Comments to Author:
Your article is now accepted for publication in J Dermatol.

Section Editor
Comments to the Author:
(There are no comments.)

Reviewer(s)' Comments to Author:

Reviewer: 1

Comments to the Author
Authors provided clear responses to my questions. I think that this revised paper is acceptable for the publication.

Reviewer: 2

Comments to the Author
The problems which I pointed out were almost cleared. Accordingly, I think that this paper is now acceptable for the publication.

Publication IV: Genital psoriasis and associated factors of sexual avoidance – a people-centered cross-sectional study in Germany

Schielein MC, Tizek L, Schuster B, Ziehfreund S, Biedermann T, Zink A. Genital Psoriasis and Associated Factors of Sexual Avoidance - A People-centered Cross-sectional Study in Germany. Acta Derm Venereol 2020; 100(10):adv00151.

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CLINICAL REPORT

Genital Psoriasis and Associated Factors of Sexual Avoidance – A People-centered Cross-sectional Study in Germany

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Patients with genital psoriasis show poorer outcomes regarding quality of life and sexual distress than those without. This study aimed to assess the occurrence of genital psoriasis and to determine factors associated with the avoidance of sexual activities due to psoriasis in a non-clinical setting. A cross-sectional, person-centered, and online-based nationwide survey was conducted in Germany between March and June 2019. A multiple logistic regression model was used to analyze the data. Furthermore, free-text answers were provided. Overall, 344 individuals with psoriasis participated. Of these, 198 (57.6%) reported having genital psoriasis and 261 (75.9%) currently received medical care. Duration of psoriasis, subjective overall severity, and pain during sex were associated with the avoidance of sexual activities. Most prevalent reasons to avoid sexual activities were 'shame,' 'pain,' and 'fear of rejection.' Sexual distress was high in this sample and a person-centered care approach needs to be further promoted.

Key words: genital psoriasis; sexual behavior; sexual health; avoidance; people-centered; person-centered.

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Acta Derm Venereol

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SIGNIFICANCE

Patients with genital psoriasis have a poorer quality of life and more sexual distress. Therefore, we conducted an online-based nationwide survey across Germany addressing persons living with psoriasis. Overall, we had 344 participants. Of these, 198 (57.6%) stated to have genital psoriasis and 83 (24.1%) did not see a doctor at the moment. Most prevalent reasons to avoid sexual activities were 'shame,' 'pain,' and 'fear of rejection.' Avoidance of sexual contact is high in individuals reached via this online-survey and needs to be further addressed. Furthermore, the approach of reaching out for persons, not patients could represent a great asset for future health care.

Psoriasis affects approximately 2% of individuals in Europe, with an enormous psychosocial component among affected individuals and their families (1–4). Psoriasis can affect all parts of the body, including the genital area (3). The reported exam-based point prevalence of genital psoriasis ranges from 12 to 42% in patients with psoriasis. However, definitions of genital psoriasis vary between the studies (5). With growing knowledge about psoriasis (6, 7), its treatment is constantly progressing, and availability of highly effective treatment is increasing (8–10). When appropriately recognized, genital psoriasis can be treated specifically and sufficiently (11, 12).

Psoriasis is associated with many comorbidities, such as depression and anxiety (1, 13, 14). Additionally, mental health might be impaired due to negative influences on sexual health (15). According to the World Health Organization (WHO), the reduction of mental health comorbidities is important to improve people's overall health (16, 17). Particularly, psoriasis patients whose genital area is affected showed an increased mental burden, poorer disease-specific quality of life, and higher sexual distress when compared to psoriasis patients without genital involvement (18–20). Although it is important that physicians assess the occurrence of genital psoriasis to prevent possible impairment of patients' sexual heath (19,20), genital involvement often remains unnoticed (20). Another problem is that not all affected individuals seek medical healthcare from a physician (21–24). Therefore, the WHO encourages the concept of people-centered care, not patient-centered care, in order to broaden the scope of research and promote public health (21, 25). Additionally, the link between genital psoriasis and the avoidance of sexual activities has not been addressed sufficiently in the existing literature (19, 26, 27).

The aims of this study were (*i*) to assess the occurrence of genital psoriasis in a non-clinical setting, and (*ii*) to determine factors associated with the avoidance of sexual activities due to psoriasis from the perspective of affected individuals.

MATERIALS AND METHODS

Study design

This cross-sectional study was designed as an online survey and carried out among individuals with psoriasis across Germany between March 2019 and June 2019. The survey was promoted on different channels (social media channels, webpages, and newsletters) by patient organizations, including "Psoriasis-Netz," "Farbenhaut," and a campaign of the Association of the German Dermatologists (BVDD), with different frequency of promotion

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and timespan of recruitment by each organization. Most people participated via "Psoriasis-Netz," which is a patient organization website providing relevant and up-to-date information for individuals affected by psoriasis or interested in psoriasis treatment. The survey was shared within their monthly e-mail newsletter, which reaches up to 2,296 registered individuals across Germany. Additionally, they shared the link for the questionnaire on their webpage and social media accounts. "Farbenhaut" and the BVDD shared the link to the questionnaire on their social media pages one month before the survey was closed. Inclusion criteria were self-reported psoriasis diagnosed by a physician (all sub-types of psoriasis) and age at time of participation of 18 years or older. The only exclusion criterion was inability to fill out a German questionnaire. Prior to participation, all individuals provided electronic informed consent. Only individuals reported having a diagnosis of psoriasis made by a physician were included in the analysis. Entries with non-plausible values or with <80% of questions answered were excluded. After completing the questionnaire, participants were directed to a page with web links that provided information about psoriasis, its comorbidities, and treatment options, as well as links to several local self-help groups across Germany. The study was approved by the local ethical committee of the Medical Faculty of Technical University of Munich (Reference: 25/19 S).

Questionnaire

The questionnaire was developed at the Technical University of Munich. Detailed information can be found in Appendix S1[1].

Statistical analysis

Data were collected using SoSci survey online tool (Version 3.2.02-i) (28). Descriptive statistics were provided for all variables. Differences between participants with or without genital psoriasis were analyzed using an unpaired *t*-test for continuous variables and a chi-square test for categorical variables. To assess factors influencing participants' tendency to avoid sexual contact due to their psoriasis, univariate and multivariate logistic regression analyses were performed. First, the role of participant characteristics (age, sex, duration of psoriasis, severity of psoriasis in general and at time point of interrogation) and specific characteristics of participants' sexual life (occurrence of genital psoriasis, relationship status, pain during sexual activities due to psoriasis) for the tendency to avoid sexual contact were tested. Second, all factors showing a significant association in univariate regression were included in the multivariate backward selection model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for both models. To avoid multicollinearity, correlations of all variables were calculated using Spearman correlations (rs) before inclusion in the multivariate model. Data management and analyses were performed using IBM SPSS Statistics 25 (IBM Corporation, Armonk, NY, USA). The level of significance (*p*-value) was set at 0.05.

Free text answers

To analyze, paraphrase, and categorize free-text answers to the question, why sexual contact was avoided, an inductive analyzing procedure using MAXQDA Analytics Pro software, version 18.0.0 (VERBI Software GmbH, Berlin, Germany) was conducted. Reasons given were subsequently categorized using an inductive approach, and categories were described quantitatively. Additionally, word counts were given for all specific words in this context, excluding non-specific words such as "the," "and," or "I."

RESULTS

Study population

A total of 351 individuals with psoriasis completed the survey and 344 were included in the presented data (Fig. S1[1]). The response rate of the institution including the most participants ("Psoriasis-Netz") was 13.9%, when considering their e-mail newsletter. The participants' mean age was 44.6 ± 13.2 years, and 59.3% of participants were women (**Table I**). Overall, 261 of 344 (75.9%) stated that they currently saw a physician due to psoriasis.

Genital psoriasis and impact on sexual activities

More than half of the participants ($n=198$; 57.6%) stated that their genital area was affected by psoriasis. Genital psoriasis was more prevalent in men than in women (65.0% vs. 52.5%; $p=0.021$), and individuals with genital psoriasis were less likely to report subjectively mild psoriasis at the time point of participation (15.2% vs. 28.1%; $p=0.007$). Overall, individuals reported an increased avoidance of sexual activities after onset of psoriasis (29.4% vs. 65.1%; Table I). No significant difference was observed between participants who later were or were not affected by genital psoriasis prior to psoriasis onset (31.8% vs. 26.0%; $p=0.238$); however, more individuals with genital involvement tended to avoid sexual activities after psoriasis onset (74.2% vs. 52.7%; $p<0.001$; Table I). The proportion of individuals stating that the question on avoidance was not applicable decreased after onset of psoriasis (23.8% vs. 9.3%). Of those participants avoiding sexual activities due to psoriasis, those with genital involvement more frequently reported to have changed their behavior from non-avoiding to avoiding (40.0% vs. 31.2%; **Fig. 1**). Of those reporting not to avoid sex due to psoriasis, most did not avoid sexual activities prior to onset either, regardless of the genital involvement (78.8–80.6%; Fig. 1). Individuals with genital psoriasis stated more often to "always" avoid sexual contact (13.6% vs. 5.5%, $p=0.001$). Furthermore, participants with genital psoriasis more frequently expressed dissatisfaction with their sex life (73.2% vs. 57.5%; $p<0.001$). More than half of all participants ($n=184$; 53.3%) stated that psoriasis influenced their choice of partner, but no significant differences were observed between the sub-groups regarding genital psoriasis.

Overall, 201 participants (71.8%) reported to avoid sexual contact at least sometimes due to their psoriasis. Correlation analysis showed fair correlations between higher age and longer duration of disease (rs 0.39; $p<0.001$) as well as between genital involvement and pain during sex (rs 0.33; $p<0.001$; Table S1[1]). Univariate analyses revealed several factors that were significantly associated with avoidance. For example, people with a longer history of psoriasis were less likely (OR 0.98,

[1]https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3509

Table I. Baseline characteristics of total study population (n=344) and stratified by psoriasis involvement of genital area

Variables	Overall (*n* = 344)	Genital area affected by psoriasis		*p*-value
		Yes (*n* = 198; 57.6%)	No (*n* = 146; 42.4%)	
Age, mean ± SD	44.6 ± 13.2	43.6 ± 13.1	45.9 ± 13.2	0.171
Sex, *n* (%)				
Women	204 (59.3)	107 (52.5)	97 (47.5)	0.021*
Men	140 (40.7)	91 (65.0)	49 (35.0)	
Do you receive medical care due to psoriasis? *n* (%)				
Yes	261 (75.9)	153 (77.3)	108 (74.0)	0.480
No	83 (24.1)	45 (22.7)	38 (26.0)	
Duration of psoriasis, mean ± SD	20.3 ± 14.2	19.4 ± 13.1	21.6 ± 15.4	0.159
Age of mean onset of psoriasis, mean ± SD	24.2 ± 14.3	24.2 ± 13.1	24.3 ± 15.8	0.985
Subjective overall severity of psoriasis, *n* (%)				
Mild	28 (8.1)	13 (6.6)	15 (10.3)	0.299
Moderate	193 (56.1)	109 (55.1)	84 (57.5)	
Severe	123 (35.8)	76 (38.4)	47 (32.2)	
Subjective severity of psoriasis at the time point of participation, *n* (%)				
Mild	71 (20.6)	30 (15.2)	41 (28.1)	0.007*
Moderate	193 (56.1)	123 (62.1)	70 (47.9)	
Severe	80 (23.3)	45 (22.7)	35 (24.0)	
Are you in a relationship? *n* (%)				
Yes	235 (68.3)	140 (70.7)	95 (65.1)	0.267
No	109 (31.7)	58 (29.3)	51 (34.9)	
Do you suffer from pain during sexual activities due to your psoriasis? *n* (%)				
Yes	154 (44.8)	116 (58.6)	38 (26.0)	<0.001*
No	135 (39.2)	59 (29.8)	76 (52.1)	
Not applicable	54 (15.7)	22 (11.1)	32 (21.9)	
Missing	1 (0.3)	1 (0.5%)	–	
Did you avoid sexual contact prior to onset of psoriasis? *n* (%)				
Yes	101 (29.4)	63 (31.8)	38 (26.0)	0.238
No	159 (46.2)	92 (46.5)	67 (45.9)	
Not applicable	82 (23.8)	41 (20.7)	41 (28.1)	
Missing	2 (0.6)	2 (1.0)	–	
Do you avoid sexual contact due to your psoriasis? *n* (%)				
Yes	224 (65.1	147 (74.2)	77 (52.7)	<0.001*
No	88 (25.6%)	36 (18.2)	52 (35.6)	
Not applicable	32 (9.3%)	15 (7.6)	17 (11.6)	
Missing	–	–	–	
Do you feel dissatisfied with your sex life due to psoriasis? *n* (%)				
Yes	229 (66.6)	154 (73.2)	84 (57.5)	<0.001*
No	112 (32.6)	52 (26.3)	60 (41.1)	
Missing	3 (0.9)	1 (0.5)	2 (1.4)	
Do you think your psoriasis has influenced your choice of partner? *n* (%)				
Yes	184 (53.3)	107 (54.0)	77 (52.7)	0.811
No	160 (46.4)	91 (46.0)	69 (47.3)	
Missing	–	–	–	

*significant with alpha of 0.05.
SD: standard deviation.

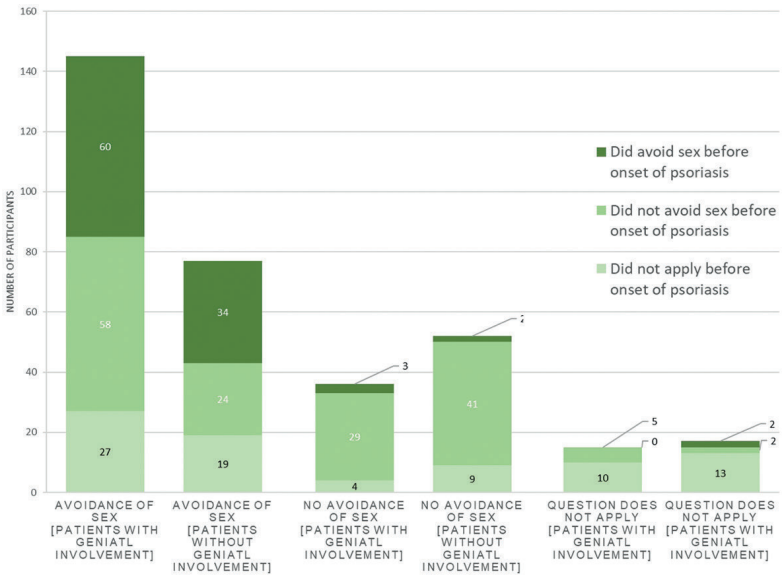

Fig. 1. Proportion of individuals avoiding sexual activities before and after onset of psoriasis. Additionally, avoidance after onset is stratified for involvement of genital area (*n* = 344).

Table II. Factors associated with avoidance of sexual contact due to psoriasis in 312 study participants

	Univariate logistic regression		Multiple logistic regression[a]	
Independent variable (reference category)	OR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Age (years)	0.98 (0.96, 1.00)	0.059		
Sex (male)	0.82 (0.50, 1.35)	0.437		
Duration of psoriasis (years)	**0.98 (0.96, 0.99)**	**0.030**	**0.97 (0.95, 0.99)**	**0.012**
subjective overall severity (mild)	**1**	**<0.001**	**1**	**0.010**
Moderate	**3.52 (1.53, 8.12)**	**0.003**	**3.49 (1.35, 9.04)**	**0.001**
Severe	**6.08 (2.48, 14.93)**	**<0.001**	**5.35 (1.93, 14.79)**	**<0.001**
Severity at time of study participation (mild)	1	0.144		
Moderate	1.53 (0.85, 2.79)	0.160		
Severe	2.07 (0.99, 4.35)	0.054		
Receiving medical care (yes)	**1.85 (1.07, 3.20)**	**0.028**		
Genital area affected by psoriasis (no)	**2.76 (1.66, 4.58)**	**<0.001**		
In a relationship (yes)	1.75 (0.99, 3.09)	0.055		
Pain during sexual activities due to psoriasis (no)	**4.18 (2.38, 7.34)**	**<0.001**	**3.41 (1.90, 6.13)**	**<0.001**

[a]*n* = 280; bold values showed significance at alpha 0.05.
OR: odds ratio; CI: confidence interval; aOR: adjusted odds ratio.

95% CI 0.96–0.99), whereas individuals with genital psoriasis (OR 2.76, 95% CI 1.66–4.58) or individuals who did not receive medical care (OR 1.85, 95% CI 1.07–3.20) were more likely to avoid sexual contact due to psoriasis. After using backward selection in the multiple logistic regression model, the remaining factors for the avoidance of sexual activities due to psoriasis were duration of psoriasis (OR 0.97, 95% CI 0.95–0.99), subjective overall moderate (OR 3.49, 95% CI 1.35–9.04) or severe psoriasis (OR 5.35, 95% CI 1.93–14.79), and pain during sexual activities due to psoriasis (OR 3.41, 95% CI 1.90–6.13) (**Table II**).

Reasons to avoid sexual activities

Overall, approximately half of the participants stating to avoid sexual activities gave a reason for doing so as free-text answers (135 of 244; 55.3%). Categorization of reasons resulted in 180 classifications within 10 categories. Double categorization was possible in cases such as "Dandruff that falls out of the hair, itchiness." Most prevalent categories were 'Shame' (*n* = 54; e.g., "Sometimes I don't feel comfortable in my skin" or "I feel ashamed"); 'Pain' (*n* = 35; e.g., "The painful open wounds around the genital area" or in many cases just "Pain"); 'Fear of rejection' (*n* = 20; e.g., "I believe that my psoriasis is repulsive for others" or "I don't want to see other people's disgusted/deterred facial expressions"); and 'Genital psoriasis' (*n* = 14; e.g., "My penis really hurts when my skin cracks from the psoriasis," and "Ashamed due to severe attack of the genital area", **Fig. 2**a). Furthermore, statements were made on stigmatization during youth (e.g., "I believe that the exclusion due to psoriasis in my childhood still negatively impacts my body image or at least negatively impacted it for a while.") and the need to explain the disease repeatedly (e.g., "The need to constantly explain my disease"). Most prevalent words used were "psoriasis" (*n* = 28), "shame" (*n* = 25), and "pain" (*n* = 24; Fig. 2b).

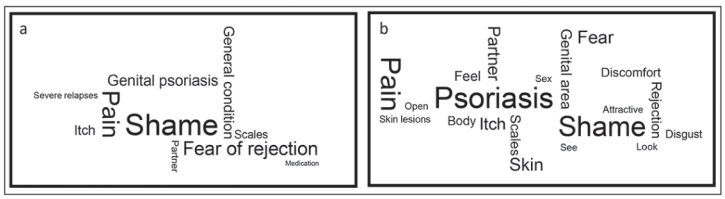

Fig. 2. Free text answers of affected individuals regarding the question for personal reasons for avoidance of sexual contact due to psoriasis. Font size in proportion to frequency of entries (actual font size equals square root of proportion times largest font size). (a) categories of reasons individuals mentioned as a reason to avoid sexual activities due to their psoriasis. Maximal mentioning: Shame, *n* = 54. (b) quantitative visualization of 20 most common words individuals mentioned during giving a reason to avoid sexual activities due to their psoriasis. Maximal mentioning: Psoriasis, *n* = 28.

DISCUSSION

The aims of the study were to assess the occurrence of genital psoriasis in a non-clinic setting and to determine factors influencing the avoidance of sexual activities due to psoriasis from the perspective of affected individuals. Of 344 participants with psoriasis, 198 had genital involvement. Individuals with genital psoriasis more frequently reported pain and avoidance of sexual activities due to their psoriasis than those without genital involvement. Furthermore, a shorter duration of psoriasis, an overall more severe psoriasis, and pain during sex were associated with the avoidance of sexual activities, which further led to sexual distress. Additional reasons included shame, pain, and the fear of rejection.

The occurrence of genital involvement was 57.6%, which is considerably higher than the rates reported previously (between 7% and 42%) (29–32). The high prevalence rate underlines the recommendation by Meeuwis et al. (19) that physicians should check for genital involvement in patients with psoriasis and pay attention to the impact of psoriasis on psychosocial aspects and sexual health. On one hand, prior studies conducted in medical settings may have underestimated the preva-

lence, as they did not include individuals who are not seeing a physician for the treatment of their psoriasis, which might be due to shame caused by genital involvement. Alternatively, the high prevalence in this study could stem from selection bias, as affected individuals might be more interested in taking part in a study about genital psoriasis. Nonetheless, in line with previous studies that have shown a prevalence of up to 42%, the prevalence in the present study may also indicate a vulnerable subgroup of individuals identified through patient organizations and non-healthcare professional settings. Additionally, the present results are in line with previous studies that report that men are more likely to develop genital psoriasis than women (20). These findings are important for dermatologists, as therapy can be optimized if knowledge of involvement of this hard-to-treat area is present. Therefore, communication with the patient about this topic is essential and barriers need to be minimized. Possible first approaches could include an improvement of physician-patient relationships or patient information on the frequency of genital psoriasis.

When considering the avoidance of sex before and after psoriasis onset, a clear change in participants' behavior occurred (Fig. 1). Interestingly, the opinion that the question on avoidance of sexual activities was not applicable decreased after the onset of psoriasis. The reason for this might include individuals not having a partner before the onset of psoriasis, or participants not thinking of avoidance before onset and therefore, stating that they could not recall. Since these are interesting points, qualitative interviews or patient journey mapping could help to better understand these highly personal transitions.

An association between disease duration and the avoidance of sexual contact was found in this study, which is contrary to the findings of Zalewska et al., who did not find this association (33). This result indicates specific coping mechanisms that may have developed during the course of disease. The implications of such mechanisms should be further investigated.

Another important point regarding avoidance of sexual activities was the perceived pain during sexual activities, which was significantly correlated with genital involvement of psoriasis. Thus, genital psoriasis could be an important indicator of sexual avoidance, even when excluded due to backward selection (34). In a previous study, Ryan et al. also showed that people with genital involvement showed impaired quality of life and sexual health (29).

Interestingly, we found that the severity of psoriasis in general was significantly associated with the avoidance of sex, while the severity at the time of study participation was not. This indicates that participants might have interpreted the question "Do you avoid sexual contact due to psoriasis?" as a general tendency rather than a current behavior; this may be why there is an association with general disease severity, but not with current disease severity. Accordingly, the avoidance of sexual contact might be a coping mechanism applied by psoriasis patients (especially those with genital involvement) which helps them to avoid feeling shame or having to explain the disease to a sexual partner (which were reasons for the avoidance of sex mentioned in free text). However, it might also indicate the importance of people's course of disease and the personal burden due to high severity, even though therapy may reduce visible symptoms. Accordingly, an additional measure of disease severity proposed by Zink et al., the lifetime highest Psoriasis Area and Severity Index (PeakPASI), may allow for more effective treatment (35). To evaluate the potential effect of this measure, more detailed and broader studies are necessary.

Free-text reasons given for the avoidance of sexual activities due to psoriasis were in line with the reasons previously reported in literature (19, 29, 36). Prior qualitatively gathered reasons like "Definitely the embarrassment… I've had one boyfriend make a comment, is that, what's this?" or "The stinging during sex, it is just a terrible feeling" seem to be confirmed by aggregated data (36). However, the inclusion of 'shame' as the most prevalent category represents the importance of internal and external stigmatization in the context of visible skin conditions (2, 37).

Study limitations and strengths

When considering generalizability of study findings, several factors should be considered. One main limitation might be a potential selection bias, including a self-selection bias. Mainly individuals who actively searched for health information regarding psoriasis, or received a newsletter or updates on social media by multiplier institutions might have participated in this survey. Additionally, a self-selection bias could have occurred as individuals with an impairment of sex life or those with genital psoriasis could react more frequently to a survey on this topic. Furthermore, study promotion via patient organization web-pages, social media accounts, and mailing systems could have led to a highly vulnerable sub-group of individuals with psoriasis. This approach might increase diversity in individuals being described in the literature as accessibility of different populations can be challenging (23). To achieve high acceptance and unbiased free-text answers, we did not use validated and extensive questionnaires to measure sexual avoidance. This might have reduced comparability and generalizability. Additionally, the response rate of the most prevalent multiplier institution was only 13.9%, when considering all individuals receiving the monthly newsletter of the patient organization, which led the most individuals to participate. This response rate seems considerably low and could have been improved by directly addressing

affected individuals, instead of only mentioning it on web pages, social media, or e-mail newsletters (38). However, it is unclear how many newsletter recipients fulfilled criteria for inclusion since subscribers also include minors, significant others or people with general interest in psoriasis. Therefore, interpretation of the response rate remains rather vague and should be considered with caution.

Furthermore, as the study was conducted online and participants stated to be diagnosed with psoriasis without control of this information, some individuals could have made incorrect statements. Even though statements were checked for plausibility by logical and time-wise criteria, the possibility of incorrect statements cannot be excluded with certainty but has to be accepted to widen the public health related horizon of populations with psoriasis. However, potential social desirability bias could have been minimized by the anonymous nature of this study. In the context of sexual content, the direct contact to a physician could have impeded participants' willingness to answer questions freely out of shame or fear to feel judged or exposed (39). Therefore, the use of an anonymous online tool might have been highly beneficial. For comparison, German individuals frequently searched for "anal itch" as a localization for occurring pruritus (20% of search queries on localized pruritus) on Google. This online search for help or information seems to be due to social norms and does not reflect patient presentations in daily clinical routine (40). Additionally, 25% of participants are highly unlikely to have been reported in literature, as they do not see a physician for their psoriasis. This result is promising and could broaden the spectrum of epidemiological descriptions.

Conclusion

The occurrence of genital psoriasis was considerably higher in this potential vulnerably subgroup of individuals with psoriasis compared to other studies, and avoidance of sex due to self-given reasons like shame, pain and fear of rejection was high. This emphasizes the importance of patient organizations when reaching out for highly vulnerable groups and individuals who do not seek medical help. Furthermore, the subjective overall severity of psoriasis was significantly associated with the avoidance of sexual activities and the inclusion of PeakPASI could be a promising influencing factor for assessing the individuals' mental impact or sexual impairment of psoriasis.

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Appendix S1

SUPPLEMENTARY MATERIAL AND METHODS

Development of the questionnaire

The questionnaire was developed at the Technical University of Munich and by a team of three epidemiologists and one dermatologist; pre-tested by three researchers and three individuals with psoriasis; and subsequently adapted to their comments. In order to minimize dropouts due to too excessive questioning on sexuality, and especially to reach unbiased qualitative reasons for the avoidance of sexual contact in the context of psoriasis, the usage of a non-validated, one-question item was chosen to determine avoidance of sexual avoidance due to psoriasis ('Do you avoid sexual contact due to your psoriasis?').

General information

Baseline characteristics of all participants were collected, which included age, sex, treating physician (general practitioner, dermatologist, rheumatologist, no current treatment), duration of psoriasis, and subjective disease severity at the time point of study participation, as well as subjective overall disease severity. Overall severity did not ask for participant's worst condition since onset of psoriasis, but for the subjective general severity over a longer time span. The term was not specified in order to leave the interpretation of this multi-dimensional construct up to the respondent, which includes visible manifestations and also quality of life aspects. Furthermore, the presence of genital involvement was measured using the question 'Is your genital area currently affected by psoriasis?'. We did not specify whether only genitals, genital and anal area, or anal area as well as groin area were affected, but left it to the interpretation of the participant.

Intimacy and avoidance of sexual contact

Furthermore, participants were provided with a questionnaire on intimacy including questions like "Do you feel pain due to your psoriasis during sexual activities? (Always–Never; 5-point scale)," or "Do you think that your psoriasis has influenced your partner search or your choice of partner?" (yes, a lot–no, 4-point scale). Participants were also asked to declare whether they avoided sexual contact since onset of psoriasis (Always–Never; 5-point scale). If they reported this as at least "sometimes," they were asked to provide a reason or reasons as free text answers on a voluntary basis. For the regression analysis, these variables were dichotomized with 'never' resulting in 'no,' and 'seldom' to 'always' resulting in 'yes'. While this might have led to a loss of information, the aim of this approach was to facilitate statistical analysis, and improve clarity and understandability of the results.

Table SI. Correlations between variables entered in the multiple regression model.

		Age	Sex	Duration of psoriasis	Subjective overall severity	Severity at time of study participation	Receiving medical care	Genital area affected by psoriasis	In a relationship	Pain during sexual activities due to psoriasis
Age	r_s	1.00	0.10	**0.39**	0.08	0.09	−0.02	−0.08	−0.08	0.07
	p-value	.	0.054	**<0.001**	0.130	0.103	0.778	0.122	0.141	0.233
Sex	r_s		1.00	0.06	0.08	0.01	0.06	**0.13**	0.08	0.02
	p-value		.	0.290	0.132	0.844	0.280	**0.021**	0.118	0.763
Duration of psoriasis	r_s			1.00	0.08	0.02	0.11	−0.05	0.05	**0.19**
	p-value			.	0.164	0.699	0.036	0.340	0.384	**0.001**
Subjective overall severity	r_s				1.00	**0.21**	**−0.17**	0.08	**0.14**	**−0.16**
	p-value				.	**<0.001**	**0.002**	0.147	**0.010**	**0.007**
Severity at time of study participation	r_s					1.000	−.073	0.09	0.03	−0.04
	p-value					.	.174	0.114	0.571	0.528
Receiving medical care	r_s						1.000	−0.04	−0.02	**0.14**
	p-value						.	0.481	0.726	**0.016**
Genital area affected by psoriasis	r_s							1.000	−0.06	**−0.33**
	p-value							.	0.268	**<0.001**
In a relationship	r_s								1.000	0.11
	p-value								.	0.053
Pain during sexual activities due to psoriasis	r_s									1.000
	p-value									.

r_s=Spearman correlation coefficient.

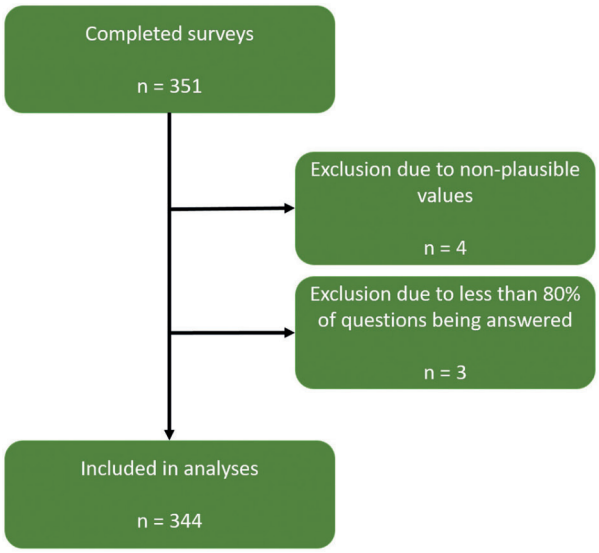

Fig. S1. Exclusion flow chart of participants before analyses.

Appendix I: Psoriasis and addictions: assessing mental health in a cross-sectional study across Germany

Schielein MC, Tizek L, Knobloch L, Maaßen D, Bidermann T, Zink A. Psoriasis and addictions: assessing mental health in a cross-sectional study across Germany; [under review]

Psoriasis and Addictions: Assessing Mental Health in a Cross-Sectional Study in Germany

Psoriasis and Addictions

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Abstract

Background

Psoriasis is a chronic skin disease with a high mental burden. Well-known comorbidities include depression, anxiety, as well as alcohol and tobacco addiction, but there is nearly no evidence on other addictions.

Objectives

The aims of this study were to estimate the prevalence of the six most common addictions among psoriasis patients in Germany and to determine associated clinical factors.

Material & Methods

Dermatologists working in four dermatological clinics and thirty-two practices across Germany recruited patients between September 2018 and November 2019. This cross-sectional study contained questionnaires on six addictions, depression, anxiety, and the Dermatology Life Quality Index (DLQI). In addition, Psoriasis Area and Severity Index (PASI) was obtained by the physicians.

Results

Overall, 502 patients (43.4% women; mean age: 49.7 ± 14.6 years) were included. Positive screenings for addictions were found in 30.3% of patients for daily smoking, 8.6% for alcohol, 1.2% for gambling, 3.8% for Internet, 3.6% for food, and 6.0% for drugs. Younger age was associated with a higher chance of a positive screening for all addictions except for alcohol dependency. The PASI was only significantly associated with smoking.

Conclusions

Addictions seem to be common among psoriasis patients. Further research should include comprehensive data and control groups. Furthermore, standardised screenings and early referrals could represent first steps to improve people-centred healthcare in psoriasis.

Keywords

Addiction Medicine, Comorbidity, Epidemiology, Mental Health, Psoriasis

INTRODUCTION

Psoriasis is a chronic inflammatory systemic skin disease associated with typical cutaneous manifestations, affecting 0.5-11.4% of the global population and 2.1% of the German population [1]. It is often accompanied by comorbidities such as cardiovascular, rheumatoid, and mental diseases [2]. Mental diseases are particularly significant in psoriasis, as psoriasis lesions often affect visible body areas or the genital area, causing stigmatisation [3, 4] and impairment of patients' quality of life, happiness, and sexual life [5–7]. Comorbid mental diseases include depression, anxiety, suicidality, and various addictions [8–13]. Addictions such as alcohol consumption and smoking are commonly investigated [10, 11], whereas data on other addictions like gambling and drug abuse are rare [12].

To improve patients' quality of life, early detection of these comorbidities is essential. However, comorbidities often remain unrecognised [14–16]. Consequently, there is a great need for improvement to reach the goals outlined in the 'Global report on psoriasis' issued by the World Health Organisation (WHO) in 2016 [17]. This report emphasised the need for people-centred care and multidisciplinary approaches in order to minimise the burden that individuals suffer due to psoriasis. When psoriasis is treated sufficiently, a reduction of disease severity has been shown to be associated with an improvement in quality of life and reduction of depressive symptoms [8, 18–20]. Since patient-physician time is limited and limited information on risk factors for mental comorbidities is available, screening for mental comorbidities is promoted in the literature [20, 21]. While some clinical risk factors for depression and anxiety are available [20–23], currently there is no evidence on risk factors for addictions.

Therefore, the aims of this study were to estimate the prevalence of the six most common addictions in Germany in patients with psoriasis and to determine clinical factors associated with the occurrence of each addiction, respectively.

MATERIALS AND METHODS

Study population

For this cross-sectional, paper-based, non-interventional study, participants were recruited from 32 dermatological practices and 4 dermatological clinics across Germany between September 2018 and November 2019. Dermatologists were invited using data from the German psoriasis physician network

79 ‘Psoriasis Praxisnetz Süd-West e.V.’. If physicians agreed to participate, they received material to
80 include up to ten patients. Additional patient sets for inclusion were provided on demand. For study
81 participation, patients had to fulfil the following inclusion criteria: aged ≥18 years, diagnosed with
82 psoriasis, able to give written informed consent, and able to answer a German questionnaire. To
83 minimise selection bias, dermatologists were asked to include either (1) the first ten psoriasis patients
84 willing to participate after start of recruitment or (2) patients who visited within the last two months
85 retrospectively and consecutively. Informed consent was obtained from every participant prior to
86 inclusion. The study and all procedures were reviewed and approved by the local ethical committee of
87 the medical faculty of Technical University of Munich (Reference 485/17 S).

88 *Questionnaire*

89 Participants received a questionnaire consisting of the German versions of nine well-established
90 questionnaires for the assessment of mental-health status. A detailed description of each measuring
91 instrument can be found in Appendix S1 and in Table 1. Dermatologists additionally documented patient
92 characteristics including age, sex, body mass index (BMI), and disease severity measured by the
93 Psoriasis Area and Severity Index (PASI).

94 *Statistics and data management*

95 Study size was limited by a patient recruitment time of one year to reduce potential seasonal influences.
96 Descriptive data were generated for general patient characteristics and prevalence of mental disorders.
97 Mental health outcomes for prevalence estimation and further analyses were defined by thresholds listed
98 in Table 1. To test differences between sex, t-test, chi-squared test, or Fisher's exact test were used.
99 Furthermore, logistic regression models were calculated to determine personal and clinical factors (age,
100 sex, BMI, Dermatology Life Quality Index (DLQI), PASI, and positive screenings for depression and
101 anxiety) that were associated with the occurrence of one of the six addictions. Variables were added to
102 multivariate regression models using backward stepwise selection to minimise multicollinearity. Odds
103 ratios (OR) and adjusted OR (aOR) were calculated with the respective 95% confidence intervals (CI).
104 Global alpha was set at 0.05. To improve the quality of the regression models, multiple imputations
105 were conducted. Therefore, a fully conditional specification method was used to impute missing data.
106 In total, five imputations were generated to calculate missing data (n=193; 3.0%). Afterwards, a

sensitivity analysis was performed to compare the results of the multiple imputation analysis with those of the complete cases (i.e., only cases without any missing data; Table S1). All data were entered twice and compared with each other to detect discrepancies. In case of error, source data were accessed and datasets were corrected. IBM SPSS Statistics (Version 25, IBM Corporation, Armonk, NY, USA) was used for all analyses.

RESULTS

Patient characteristics

A total of 502 participants were included in this study. The mean age was 49.7 years (±14.6 years) and 218 (43.4%) were women. The mean BMI was 28.1 (±5.4) and the mean PASI was 7.3 (±7.6). Mean DLQI was 7.5 (±7.1), with a significantly higher impairment in women than in men (8.4±7.3 vs. 6.8±7.0, p=0.020). Nearly half of all patients (44.8%) reported no or a small effect of psoriasis on their daily life, whereas 27.1% reported a large or extremely large impact. Overall, 29.5% of individuals screened positive for depression, with 11.4% indicating major depression. Anxiety was found in 48.8% of patients, with 17.5% having signs for an anxiety disorder (Figure 1). Women were more likely to have a positive screening result for depression (35.8% vs. 24.7%, p=0.006) and anxiety disorder than men (20.1% vs. 14.8%; p<0.001, Table 2).

Prevalence of addictions

A total of 152 participants (30.3%) reported daily cigarette smoking, with no significant difference between women and men (33.0% vs. 28.2%, p=0.216, Table 2). The mean duration of daily smoking was 24.2 years (±13.1 years). Of those who are smoking daily, 55.3% (n=84) stated that they smoked less than a pack per day, 34.9% (n=53) one pack per day, and 9.9% (n=15) more than a pack per day. Additionally, 8.6% (n=43) of all patients screened positive for alcoholism, with a higher proportion in men than women (11.3% vs. 5.0%, p=0.020). A sex difference was also observed regarding gambling addiction as only men showed positive screening results (2.2% of men vs. 0% of women, p=0.039). For all other addictions, no sex difference was found. Overall, 3.8% (n=19) of the patients showed pathological Internet behaviour and 2.0% (n=10) had a borderline to pathological Internet consumption. Around 3.6% (n=18) of the patients screened positive for food addiction. Furthermore, 15.0% (n=75) displayed at least a low level of abusive behaviour regarding drugs, with a positive screening of 6.0%

(n=30) for drug abuse (Figure 1). When considering any addiction, 36.9% (n=185) of patients screened positive for at least one addiction, with no significant differences in sex (women: 37.6% vs. men: 36.2%, p=0.200). However, when examining the number of addictions, women were more likely to have one addiction (30.7% vs. 24.3%), while men were more like to have two or more addictions (11.9% vs. 6.9%, p=0.013; Table 2).

Associated factors for addictions

Expect for alcohol dependency, younger age was associated with a higher chance for a positive screening for each addiction. Thereby, age had the strongest influence on pathological gambling (OR_{MI} = 0.93, 95% CI 0.87-1.00) and drug addiction (OR_{MI} = 0.94, 95% CI 0.92-0.97, Figure 1). Additionally, the PASI was positive associated with smoking (OR_{MI} = 1.04, 95% CI 1.01–1.07). For example, a ten-point increase in PASI was associated with a 40% increase in the chance of smoking. Furthermore, depression was significantly associated with alcohol (OR_{MI} = 2.66, 95% CI 1.40-5.01) and drug addiction (ORMI = 2.66, 95% CI 1.23-5.77), whereas chances for Internet (OR_{MI} = 7.66, 95% CI 2.92-19.98) and food addiction (OR_{MI} = 3.03, 95% CI 1.10-8.36) were higher in patients with a positive screening for an anxiety disorder (Table S1).

DISCUSSION

The aim of this study was to provide evidence on the estimated prevalence of six addictions in patients with psoriasis as well as to identify associated clinical factors. Overall, mental burden was high in patients with psoriasis and there was a high prevalence of addiction with nearly half of the patients reporting signs for at least one addiction. Especially, Internet addiction was surprisingly high in the study population. Younger age was associated with a higher chance for the occurrence of most addictions.

Comparison to the general population

The study's finding indicated that psoriasis patients have a greater likelihood of several addictions compared to representative samples of the German general population, including daily smoking (30.3% vs. 15.1%) [24], alcohol dependency (8.6% vs. 3.1%) [24], pathological gambling (1.2% vs. 0.2%) [25], and legal or illegal drugs abuse (6.0% vs. 3.2%-5.2%) [24]. The increased mental burden due to skin diseases and social withdrawl might play important roles in this association [13, 26]. Despite the higher

BMI in this sample compared to the general population (28.1 vs. 26.7), food addiction was found to be less prevalent among patients with psoriasis (3.6% vs. 7.9%) [27], although the logistic regression revealed a positive association with the BMI. This difference could indicate either a reason other than excessive eating for weight gain in psoriasis patients or the presence of a social desirability bias.

Internet addiction is reported to decrease with rising age [28, 29], however, pathological Internet use was higher in this study (3.8%), where the patients' mean age was 49.7 years, than in a study including a representative sample of German adolescents with a mean age of 14.9 years (3.2%) [30]. Another study performed by Rumpf et al. assessed the Internet addiction among more than 8,130 German individuals, who had a mean age of 39.9 years and used the Internet regularly [28]. When adjusted to the cut-off used by Rumpf et al., the prevalence for Internet addiction was equal in both studies (1.5%), although this study population was older. Accordingly, the study's findings might indicate an association of Internet addiction with psoriasis, which requires further investigation.

Comparison to other studies on individuals with psoriasis

The proportion of psoriasis patients that currently smoke varies widely in the literature, ranging from 14.0% to 51.3% [10]. Although the prevalence detected in this study was within this range, it was lower compared to that reported in another German study among psoriasis patients (30.8% vs. 41.0%) [12]. In a systematic review, the prevalence of alcohol addiction was reported to be between 11.1% and 28.0% in psoriasis patients [11], which is higher than that reported in this study. One study that also used the CAGE score to assess alcohol addiction reported a prevalence of 18.3% among psoriasis patients [31]. A reason for that considerable higher prevalence might be the fact that only 60 patients with psoriasis were investigated. Another study including psoriasis patients from a dermatological clinic and also assessing alcohol dependency via the CAGE questionnaire reported an estimated prevalence of 13.5% [12]. Although the prevalence of alcohol addiction was lower in this study compared to most of the previous studies, the prevalence I exceeded the rate found within the German general population (3.1% [24]).

In comparison to the general population, the prevalence of Internet addiction was higher among the included psoriasis patients, however the prevalence was lower in comparison to another study including individuals with psoriasis reached via online self-help groups (8.5%) [26]. As the prevalence was even higher in people with psoriasis than in patients with psoriasis, the results underline the importance of a people-centred care as demanded by the WHO [17].

When considering compulsive gambling, food addiction, and drug abuse, reported data on individuals with psoriasis are limited to one study performed by Zink et al., which included 102 patients from a university hospital [12]. While compulsive gambling was higher than in the present sample (2.0% vs. 1.2%), food addiction (3.1% vs. 3.6%) and drug addiction (1.0% vs. 2.4%; threshold adapted to Zink et al.) were lower than in this sample. As there were no considerable differences regarding age and severity of psoriasis, the different findings emphasise the need for further clarification and research potentially including data extracted from health insurances.

Although patients included in this study had lower values for PASI and DLQI compared to a study by Lamb et al. [18], the prevalence found for depression and anxiety were higher than in the other study, who found that 9.9% of their psoriasis patients were likely to have major depression and 13.1% a generalised anxiety disorder. Another study by Delgard et al. [32] found a comparable prevalence of 13.8% for depression, but a higher prevalence for anxiety (22.7%). Interestingly, Delgard et al. reported depression and anxiety to exhibit aORs of 3.0 and 2.9 in patients with psoriasis when compared with healthy controls, which emphasises the mental impairment caused by psoriasis [32].

Associated factors for addictions

There was no previous study that investigated individual and clinical factors associated with all the six addictions. The multiple regression models revealed that for most of the addictions, younger age had a significantly influence. Although age is discussed highly controversial in terms of addiction within the current literature [33, 34], it stands out that for all addictions, expect for alcohol addiction, the chance of being screened positive significantly decreased with rising age. While being controlled via backward selection, only daily smoking was associated with a higher PASI. This might either indicate the absence of a classical dose-response relationship or that conventional strategies to classify disease severity in a cross-sectional manner might not comprehensively reflect the individual burden experienced by patients [35]. Furthermore, all addictions apart from smoking and gambling were associated with depression or anxiety, which is in accordance with the literature [36]. These findings strengthen the reliability of the study results. However, no certain clinical factor can be identified as potential predictor and reported prevalence remain higher than those reported within the general population. Therefore, the findings also emphasise the need for further research and standardized screenings.

Strengths and limitations

A major strength of this study is the large number of patients and a strict set of rules for consecutive inclusion of patients was applied to reduce selection bias. Additionally, recruitment was carried out in 36 medical settings throughout Germany. There are some study limitations, however. First, there is a potential for selection bias as participation for dermatologists was voluntary and this can lead to a self-selected subgroup of dermatologists. Second, screening for addictions was performed using standardised questionnaires without a corresponding control group, so that comparisons are only indirect. Although the questionnaires are validated and all showed acceptable results for specificity and sensitivity [3], it has to be taken into account that these findings do not represent diagnoses but rather estimate the respective outcomes. Third, a certain degree of social and desirability bias needs to be considered. Patients are not always willing to disclose information regarding sensitive and potentially stigmatising data [37, 38].

Conclusion

In conclusion, the prevalence of addictions, especially Internet addiction, was high among patients with psoriasis. To verify the association between the prevalence and psoriasis, future research should also include a suitable control group or claims data. The study findings underline the importance of implementing a routine, not too time-consuming assessments of psychological comorbidities when assessing psoriasis severity, which could be easily implemented in psoriasis care [21–23]. As different clinical variables were associated with the occurrence of different addictions, a possible first step could include routine and standardised screening as well as referral for early detection and treatment of these psychological disturbances to improve the quality of people-centred care.

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Conflict of Interest: MCS received speaker's honoraria and/or were financially supported for the presentation of scientific posters by Janssen-Cilag, Novartis. LT was financially supported for the presentation of scientific posters by Novartis Pharma GmbH. LK has no conflict of

interest to declare. DM has served as a consultant and/or paid speaker for and/or has received honoraria for consulting and/or got travel expenses reimbursed and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis including AbbVie, Almirall, Amgen, Biogen (Biogen Idec), Celgene, Eli Lilly, Janssen-Cilag, Leo, Medac, MSD (formerly Essex, Schering-Plough), Mundipharma, Novartis, Pfizer (formerly Wyeth), USB. TB gave advice to or got an honorarium for talks or research grant from the following companies: Celgene, Novartis, Lilly. AZ has been an advisor and/or received speaker's honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Almirall, Celgene, Eli Lilly, Janssen-Cilag, Novartis.

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FIGURES

Figure 1: Prevalence of positive screenings for depression, anxiety and the six most common addictions in Germany (smoking, alcohol, gambling, Internet, food, drugs). Results overall and stratified by gender.

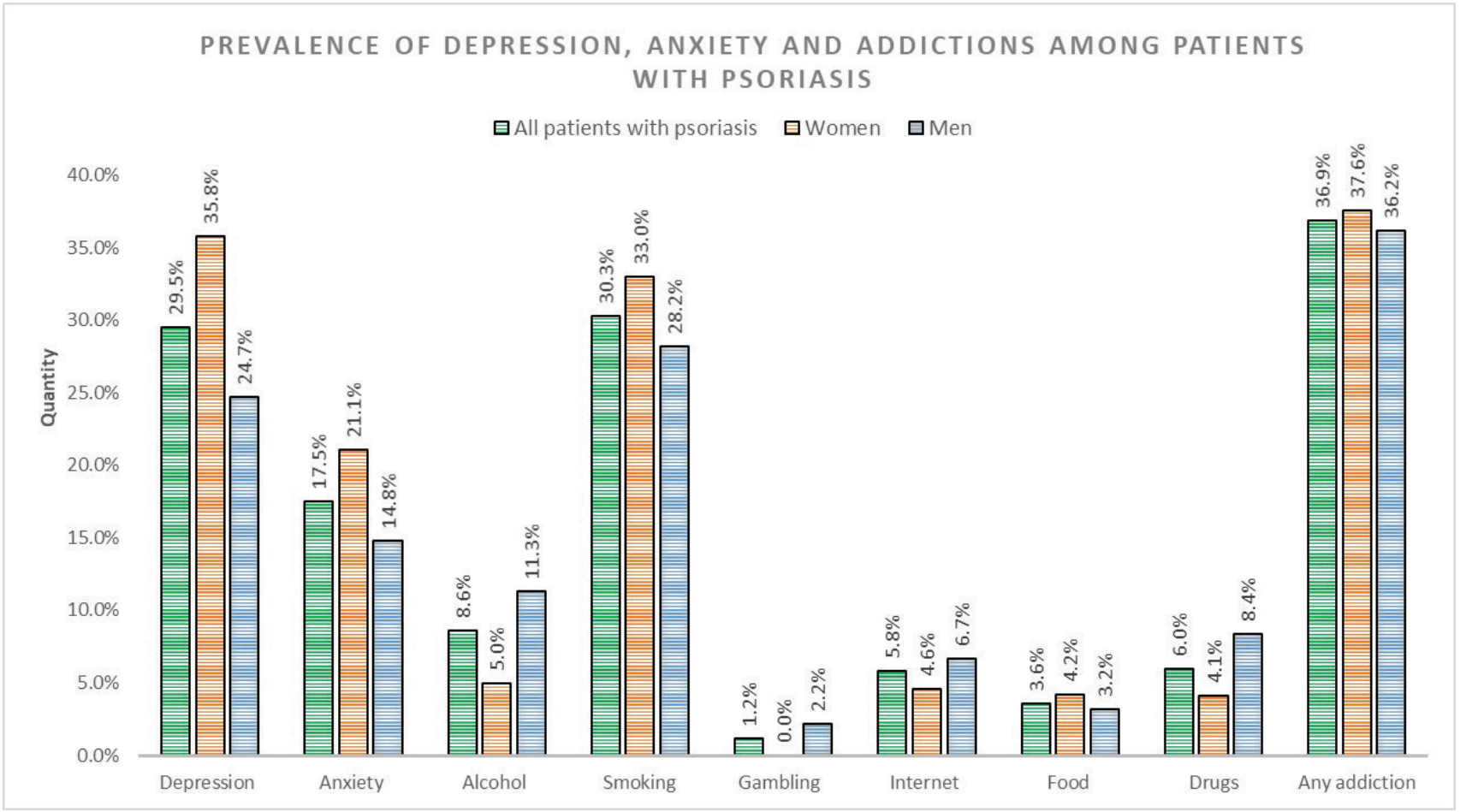
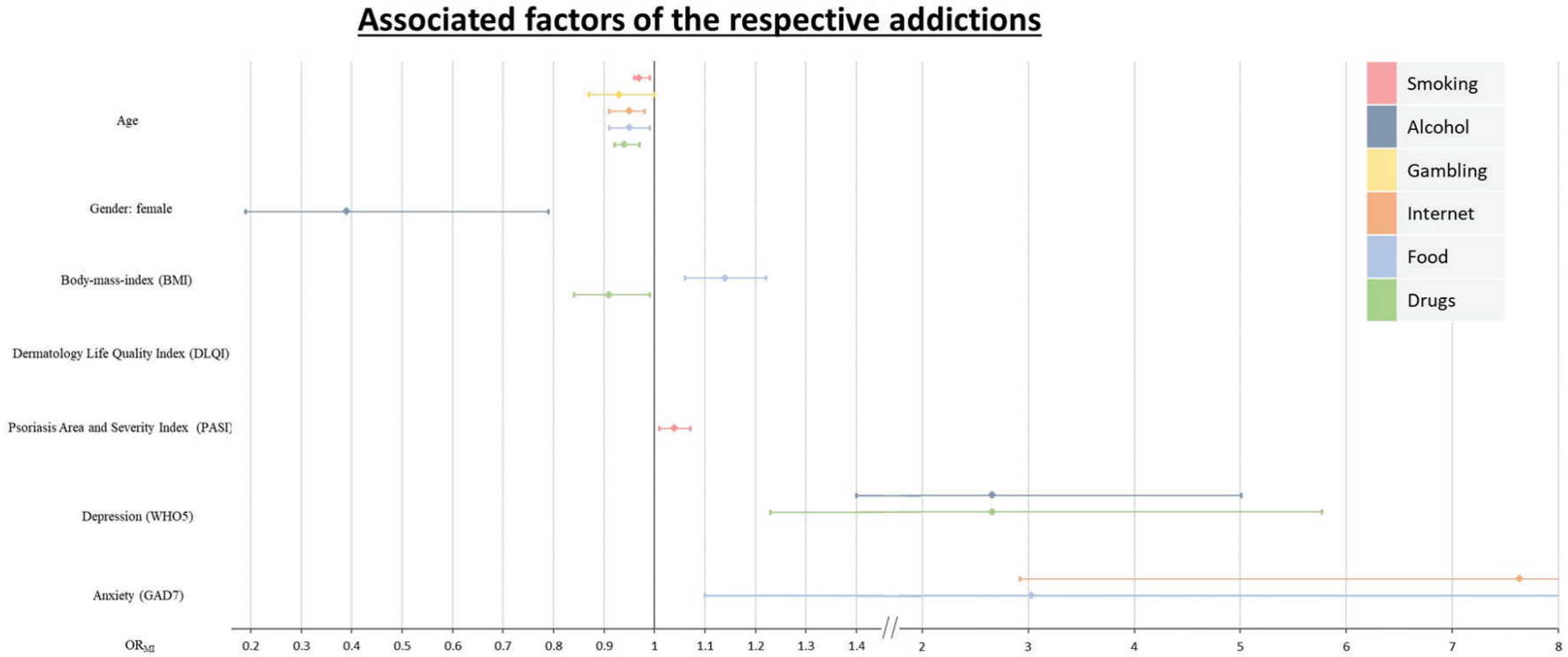


Figure 2: Personal and clinical factors associated with the positive of each least one addiction. BMI=Body-Mass-Index; DLQI=Dermatology Life Quality Index; PASI = Psoriasis Area and Severity Index; WHO5=WHO-Five Well-Being Index; GAD-7=Generalized Anxiety Disorder 7-item.



343 **TABLES**

344 Table 1: Standardised questionnaires included in study questionnaire.

Questionnaire	Abbreviation	Number of questions	Scale	Possible answers (value)	Range	Classifications
Dermatology Life Quality Index	DLQI	10	ordinal[a]	[ ] very much (3) [ ] a lot (2) [ ] a little (1) [ ] not at all (0) [ ] not relevant (0)	0-30	[0-1] no effect at all on patient's life [2-5] small effect on patient's life [6-10] moderate effect on patient's life [11-20] very large effect on patient's life [21-30] extremely large effect on patient's life
WHO-Five Well-Being Index	WHO5	5	ordinal	[ ] at no time (0) [ ] some of the time (1) [ ] less than half of the time (2) [ ] more than half of the time (3) [ ] most of the time (4) [ ] all of the time (5)	0-100	[100-51] good wellbeing [50-29] depressive tendency/depression* [28-0] potentially major depression*
Generalized Anxiety Disorder 7-item	GAD-7	7	ordinal	[ ] not at all (0) [ ] several days (1) [ ] over half the days (2) [ ]nearly every day (3)	0-21	[0-4] good wellbeing [5-9] mild anxiety [10-14] moderate anxiety* [15-21] severe anxiety*
CAGE-questionnaire	CAGE	4	binominal	[ ] yes (1) [ ] no (0)	0-4	[0-1] no drinking problem [2-4] alcohol use disorder*
Gamblers Anonymous 20 Questions	20Q	20	binominal	[ ] yes (1) [ ] no (0)	0-20	[0-6] no gambling problem [7-20] compulsive gambling*
Compulsive Internet Using Scale	CIUS	14	ordinal	[ ] never (0) [ ] seldom (1) [ ] sometimes (2) [ ] often (3) [ ] very often (4)	0-56	[0-17] not problematic [18-20] borderline [21-56] pathological internet use*

Modified Yale food addiction scale 2.0	mYFAS 2.0	13	ordinal	[ ] never (0) [ ] less than 1 time a month (1) [ ] once a month (2) [ ] 2-3 times per month (3) [ ] once a week (4) [ ] 2-3 times per week (5) [ ] 4-6 times per week (6) [ ] daily (7)	0-11[b]	[0-1] no eating disorder [2-3][c] mild eating disorder* [4-5][c] moderate eating disorder* [6-11][c] severe eating disorder*
Drug Abuse Screening Test	DAST-10	10	binominal	[ ] yes (1) [ ] no (0)	0-10	[0] no problem indicated [1-2] low level [3-5] moderate level* [6-8] substantial level* [9-10] severe level*

*Considered clinically significant

[a] Question seven differs and is a combination of binominal and ordinal scales.

[b] Each item has an individual classification of being present (1) or not (0). Range over all items for being present (1) is from [2-7] to [5-7], respectively.

[c] Plus impairment or distress items which were fulfilled if being present at least 2-3 times per week.

Table 2: General characteristics of participants stratified by sex. Differences were compared using unpaired t-test and Chi square test. SD=Standard deviation; BMI=Body-Mass-Index; DLQI=Dermatology Life Quality Index; PASI=Psoriasis Area and Severity Index. Significant results printed bold.

		Total (n=502)		**Women (n=218)**		**Men (n=284)**		**P-value**
		[n (%)]	**Mean ± SD**	**[n (%)]**	**Mean ± SD**	**[n (%)]**	**Mean ± SD**	
Age			49.7 ± 14.6		50.7 ± 14.8		48.9 ± 14.4	0.164
BMI			28.1 ± 5.4		28.3 ±6.5		28.0 ± 4.3	0.594
PASI			7.3 ± 7.6		6.7 ± 6.8		7.8 ± 8.1	0.098
DLQI			7.5 ± 7.1		8.4 ± 7.3		6.8 ±7.0	**0.020**
Depression	No	351 (69.9)		139 (63.8)		212 (75.2)		**0.006**
	General	91 (18.1)		43 (19.7)		48 (17.0)		
	Major	57 (11.4)		35 (16.1)		22 (7.7)		
	Missing	*3 (0.6)*		*1 (0.5)*		*2 (0.7)*		
Anxiety	No	248 (49.4)		84 (38.5)		164 (57.7)		**< 0.001**
	Mild	157 (31.3)		83 (38.1)		74 (26.1)		
	Moderate	68 (13.5)		36 (16.5)		32 (11.3)		
	Severe	20 (4.0)		10 (4.6)		10 (3.5)		
	Missing	*9 (1.8)*		*5 (2.3)*		*4 (1.4)*		
Daily smoking	Yes	152 (30.3)		72 (33.0)		80 (28.2)		0.216
	No	343 (68.3)		142 (65.1)		201 (70.8)		
	Missing	*7 (1.4)*		*4 (1.8)*		*3 (1.1)*		
Years of smoking			24.2 ± 13.1		25.3 ± 13.3		23.3 ± 12.9	0.355
Alcohol	Yes	43 (8.6)		11 (5.0)		32 (11.3)		**0.020**
	No	444 (88.4)		195 (89.4)		249 (87.7)		
	Missing	*15 (3.0)*		*12 (5.5)*		*3 (1.1)*		

Gambling	Yes	6 (1.2)	0 (0.0)	6 (2.1)	**0.039***
	No	481 (95.8)	210 (96.3)	271 (95.4)	
	Missing	*15 (3.0)*	*8 (3.7)*	*7 (2.5)*	
Internet	No	449 (89.4)	195 (89.4)	254 (89.4)	0.583
	Borderline	10 (2.0)	4 (1.8)	6 (2.1)	
	Pathological	19 (3.8)	6 (2.8)	13 (4.6)	
	Missing	*24 (4.8)*	*13 (6.0)*	*11 (3.9)*	
Food	No	475 (94.6)	205 (94.0)	270 (95.1)	0.423
	Mild	7 (1.4)	5 (2.3)	2 (0.7)	
	Moderate	4 (0.8)	1 (0.5)	3 (1.1)	
	Severe	7 (1.4)	3 (1.4)	4 (1.4)	
	Missing	*9 (1.8)*	*4 (1.8)*	*5 (1.8)*	
Drugs	No	406 (80.9)	174 (79.8)	232 (81.7)	0.484
	Low level	45 (9.0)	22 (10.1)	23 (8.1)	
	Moderate level	18 (3.6)	5 (2.3)	13 (4.6)	
	Severe level	8 (1.6)	2 (0.9)	6 (2.1)	
	Substantial level	4 (0.8)	2 (0.9)	2 (0.7)	
	Missing	*21 (4.2)*	*13 (6.0)*	*8 (2.8)*	
Addictions	None	250 (49.8)	95 (43.6)	155 (54.6)	***0.013***
	One	136 (27.1)	67 (30.7)	69 (24.3)	
	Two	36 (7.2)	14 (6.4)	22 (7.7)	
	Three or more	13 (2.6)	1 (0.5)	12 (4.2)	
	Missing	*67 (13.3)*	*41 (18.8)*	*26 (9.2)*	

353 *Fisher's exact test was used as requirements for Chi square test were not fulfilled.

SUPPLEMENTARY MATERIAL

Table S1: Results of the complete-case analysis compared to the multiple imputation analysis assessing clinical factors associated with the positive screening for depression, anxiety or addictions.

Dependent variable	Independent variables (reference)	Crude OR_{CC}	Adjusted OR_{CC} (95% CI)	Adjusted OR_{MI} m = 5 (95% CI)	Change in ß-Coefficient
Daily smoking *N_{CC} = 418* *N_{MI} = 502*	Age	**0.97 (0.96-0.99)**	**0.98 (0.96-0.99)**	**0.97 (0.96-0.99)**	0.12
	Gender (male)	1.27 (0.87-1.87)			
	BMI	0.98 (0.94-1.02)			
	DLQI	**1.04 (1.01-1.07)**			
	PASI	**1.03 (1.01-1.06)**	**1.03 (1.01-1.06)**	**1.04 (1.01-1.07)**	0.18
	Depression	**1.72 (1.15-2.59)**			
	Anxiety	1.38 (0.85-2.24)			
Alcohol dependency *N_{CC} = 413* *N_{MI} = 502*	Age	0.99 (0.97-1.01)			
	Gender (male)	**0.44 (0.22-0.89)**	**0.41 (0.19-0.90)**	**0.39 (0.19-0.79)**	0.07
	BMI	0.99 (0.93-1.06)			
	DLQI	1.01 (0.97-1.06)			
	PASI	1.03 (0.99-1.07)			
	Depression	**2.30 (1.22-4.34)**	**3.06 (1.51-6.20)**	**2.66 (1.40—5.01)**	-0.12
	Anxiety	1.93 (0.95-3.94)			
Pathological gambling *N_{CC} = 414* *N_{MI} = 502*	Age	**0.94 (0.87-1.00)**	**0.91 (0.84-0.99)**	**0.93 (0.87-1.00)**	-0.26
	Gender (male)	N/A			
	BMI	0.84 (0.47-1.05)			
	DLQI	1.05 (0.95-1.16)			
	PASI	1.00 (0.91-1.11)			

	Depression	1.23 (0.22-6.80)			
	Anxiety	4.70 (0.93-23.69)			
Internet addiction *N_{CC} = 404* *N_{MI} = 502*	Age	**0.95 (0.91-0.98)**	**0.95 (0.91-0.99)**	**0.95 (0.91-0.98)**	0.06
	Gender (male)	0.60 (0.23-1.61)			
	BMI	1.02 (0.94-1.11)			
	DLQI	1.04 (0.98-1-11)			
	PASI	0.99 (0.92-1.06)			
	Depression	2.22 (0.88-5.58)			
	Anxiety	**6.88 (2.68-17.67)**	**4.81 (1.71-13.50)**	**7.63 (2.92-19.98)**	0.29
Food addiction *N_{CC} = 414* *N_{MI} = 502*	Age	**0.96 (0.92-0.99)**	**0.94 (0.90-0.98)**	**0.95 (0.91-0.99)**	0.19
	Gender (male)	1.32 (0.51-3.38)			
	BMI	**1.14 (1.06-1.22)**	**1.13 (1.05-1.21)**	**1.14 (1.06-1.22)**	0.04
	DLQI	**1.07 (1.01-1.13)**			
	PASI	1.02 (0.96-1.07)			
	Depression	1.22 (0.45-3.32)			
	Anxiety	**3.92 (1.50-10.24)**	**3.74 (1.28-10.94)**	**3.03 (1.10-8.36)**	-0.16
Drug addiction *N_{CC} = 411* *N_{MI} = 502*	Age	**0.94 (0.91-0.97)**	**0.94 (0.91-0.97)**	**0.94 (0.92-0.97)**	-0.12
	Gender (male)	0.56 (0.25-1.24)			
	BMI	**0.91 (0.83-0.99)**	**0.92 (0.84-1.00)**	**0.91 (0.84-0.99)**	0.07
	DLQI	**1.07 (1.02-1.12)**			
	PASI	**1.04 (1.00-1.09)**			
	Depression	**2.56 (1.21-5.38)**		**2.66 (1.23-5.77)**	N/A
	Anxiety	**2.42 (1.09-5.38)**	**3.81 (1.54-9.42)**		N/A

OR = odds ratio, CI = confidence interval; CC = complete-case (cases with missing values were excluded); MI = multiple imputation; m = number of imputations; BMI = Body-Mass-Index; DLQI=Dermatology Life Quality Index; PASI = Psoriasis Area and Severity Index. N/A = Not applicable Significant results printed bold.

Appendix S1. Supplementary information on questionnaire methodology

Dermatology Life Quality Index

Disease-specific quality of life was measured using the Dermatology Life Quality Index (DLQI; Cronbach's α = 0.75-0.92) [1–3]. It is a commonly used questionnaire including 10 questions such as 'Over the last week, how itchy, sore, painful, or stinging has your skin been?' and 'Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?'. Questions can be answered on a scale ranging from 'not at all' (0) to 'very much' (3) and the scale ranges from a minimum of 0 to a maximum of 30. Overall, the range from 0 to 1 indicates 'no effect at all on patient's life', while 2 to 5 indicates a mild, 6 to 10 a moderate, 11 to 20 a large, and 21 to 30 an extremely large effect on the patient's life [1].

World Health Organization (WHO)-Five Well-Being Index

Depression was assessed using the International Classification of Diseases (ICD)-10-based WHO-Five Well-Being Index (WHO5, Cronbach's α = 0.88) [4–6]. It is a validated, standardised, and widely used questionnaire consisting of five questions on an individual's wellbeing like 'I have felt calm and relaxed' or 'My daily life has been filled with things that interest me'. Answers range from 'All of the time' (5) to 'At no time' (0), and all answers are multiplied by 4 to reach a score between 0 and 100. Lower values indicate a poorer outcome for the individual's well-being. When used as a screening tool for depression, it yields a sensitivity of 0.86 and a specificity of 0.81 at a cut-off value of ≤50 for depression [4] and a sensitivity of 0.94 and a specificity of 0.83 for a cut-off value of ≤28 for major depression [7]. Therefore, estimations for both cut-offs were calculated.

Generalized Anxiety Disorder 7-item Assessment

The Generalized Anxiety Disorder 7-item (GAD-7, Cronbach's α = 0.89) scale was used for the assessment of anxiety [8, 9]. It contains seven questions considering the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria containing questions on topics like having trouble relaxing and becoming easily annoyed or irritable. Each question is ranked on a 4-point Likert scale ranging from 'Not at all' (0) to 'Nearly every day' (3). Accordingly, the score ranges between 0 and 21. It distinguishes between mild (5-9), moderate (10-14), and severe (15-21) anxiety. For further analyses, a cut-off point of 10 or higher was defined to determine the presence of a generalised anxiety disorder. This cut-off value previously showed a sensitivity of 89% and a specificity of 82% [9].

CAGE-questionnaire

A possible alcohol use disorder was determined using the DSM-based CAGE-questionnaire (CAGE, r = 0.89 at presented cut-off) [10, 11]. The letters in CAGE refer to the initial letters of the 4 respective questions. The questionnaire addresses an individual's drinking behaviour, focusing on 'Cutting down', 'Annoyed by criticism', 'Guilt about drinking', and alcohol as an 'Eye-opener' in the morning. If at least two of these questions were answered with 'yes', the patient was considered as potentially having an alcohol use disorder. The questionnaire yields an average sensitivity of 0.71 and specificity of 0.90 [12].

Smoking

Smoking was assessed by the question 'Do you smoke?'. Participants were subsequently asked to declare whether they smoked 'seldom', 'daily, less than a pack, 'daily, one pack of cigarettes', 'daily, 1.5 packs of cigarettes', or 'daily, more than 2 packs of cigarettes'. A pack of cigarettes was predefined as 20 cigarettes. Participants with daily smoking habits were considered as smokers for further analyses. All participants who smoke were additionally asked to declare for how many years they have been smoking.

Gamblers Anonymous 20 Questions

The occurrence of a pathological gambling behaviour was determined using the Gamblers Anonymous 20 Questions (20Q, Cronbach's $\alpha = 0.84\text{-}0.94$) [13, 14]. This questionnaire is comparable to the DSM-IV diagnostic criteria and contains 20 questions on an individual's gambling habits. Answers are dichotomous and add up to a score ranging from 0 (all questions answered no) to 20 (all questions answered yes). The cut-off for this instrument was set to ≥ 7 as proposed in the literature [14]. Subsequently, individuals answering seven or more questions with yes were considered addicted to gambling.

Compulsive Internet Use Scale

Pathologic behaviour regarding Internet use was quantified by the Compulsive Internet Use Scale (CIUS; Cronbach's $\alpha = 0.93$) [15, 16]. The questionnaire contains 14 questions in the subcategories 'loss of control', 'preoccupation (including behavioural and mental factors)', 'withdrawal symptoms', 'coping or mood modification', and 'conflict'. Answers were given on a 5-point Likert scale ranging from 'never' (0) to 'very often' (4). The scale ranges from 0 to 56 and the cut-offs for borderline use and pathological Internet use were ≥ 18 and ≥ 21, respectively. Higher values indicate higher addiction to the Internet.

Modified Yale Food Addiction Scale 2.0

For the occurrence of any food addiction or eating disorder, the abbreviated version of the Yale Food Addiction Scale 2.0 (mYFAS 2.0, Kuder–Richardson $\alpha = 0.86$) was used [17]. It contains questions focusing on relevant DSM-V criteria such as 'I ate to the point where I felt physically ill' and 'I tried and failed to cut down on or stop eating certain foods'. It describes 11 symptoms, and two items survey impairment and distress. Items are answered using a 7-point scale ranging from 'Never' (0) to 'Daily' (7) and classification for relevance differs between items. Therefore, some items are deemed relevant if they are answered with (2) to (7) (e.g. items 6 and 12), while others are deemed relevant if answered with (4) to (7) (e.g. items 4 and 8) or (5) to (7) (e.g. items 2 and 5). The computed score of symptoms ranges from 0 to 11. If at least one item describing impairment or distress was present at least 2 to 3 times per week, a score of 2 to 3 could be considered as a mild, a score of 4 to 5 as a moderate, and a score of 6 to 11 as a severe eating disorder. For further analyses, the combination of impairment or distress plus a score of 2 or higher was considered 'diagnostic' for a food addiction [17, 18].

Drug Abuse Screening Test

The Drug Abuse Screening Test (DAST-10, Cronbach's $\alpha = 0.86$-0.94) was used to screen for drug abuse [19–21]. The DAST-10 contains questions like 'Have you used drugs other than those required for medical reasons?' and 'Have you engaged in illegal activities in order to obtain drugs?' and is based on DSM-III criteria. Questions are answered with either yes or no. Item number 3 ('Are you always able to stop using drugs when you want to?') was coded reverse. If participants indicated not using illegal drugs, but responded 'no' to that question, the answer was not counted. Subsequently, no positive answer indicated no problem, whereas 1 to 2 positive answers indicated a low, 3 to 5 a moderate, 6 to 8 a substantial, and 9 to 10 a severe problem [19, 20]. For further analyses, a cut-off value of 3 or more positive answers was considered as a positive screening result [20, 21].

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Appendix II: Stigmatization caused by hair loss – a systematic literature review

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Stigmatization caused by hair loss – a systematic literature review

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Summary

Hair loss is a symptom that can cause stigmatization and severe impairment of quality of life. The aim of this systematic review was to evaluate the literature on stigmatization of hair loss. Using predefined MeSH terms and keywords, a systematic search was performed in the databases MEDLINE (PubMed), EMBASE, PsycINFO and PsycNET. No time restriction was chosen (last update: May 07, 2019; PROSPERO registration number: CRD42019122966). A total of 98 studies were identified, of which eleven were selected for inclusion in this work. The Hairdex, a questionnaire on disease-specific quality of life, was the most frequently used instrument for the quantitative assessment of stigma. The studies were highly heterogeneous and values for stigmatization of androgenetic alopecia varied widely. However, regardless of the pathogenesis, patients with hair loss often suffer from stigmatization which limits their quality of life. Stigmatization of people with visible skin lesions has often been neglected in clinical practice and in daily contact with affected individuals. Studies that specifically address the stigma of hair loss are rare. Further studies are needed to achieve comparability within pathogeneses as well as with other visible dermatoses in order to better understand the enormous psychosocial burden of hair loss.

Background

Hair loss is, irrespective of its pathogenesis or severity, a cause of distress for affected individuals that is often underestimated by outside parties [1–3]. Pathogeneses vary and include androgenetic alopecia, alopecia areata, diffuse alopecia, and therapy-induced hair loss [4, 5]. While modern therapies are on the advance [6–8], affected individuals often suffer from internalized and external stigmatization in addition to a reduced quality of life and a large number of psychological comorbidities due to their changed appearance [4, 9]. Stigmatization describes a phenomenon that excludes affected individuals from complete social acceptance. This phenomenon may be triggered by the patients themselves (internalized stigma), or it may be induced by their environment (external stigma) [10]. Given the heavy burden on affected individuals, stigmatization may then result in psychological diseases [4] and severely impair the quality of life [11]. Dermatological disorders are common [12], and because of stigmatization in case of visible skin changes and its impact on the life of many affected individuals, the German Federal Ministry of Health (BMG) initiated the project initiative "*In meiner Haut*" (in my skin) for the destigmatization of people with visible skin alterations [13]. In this context, an expert panel consisting of patient representatives, scientists and physicians currently develops and scientifically evaluates various formats of intervention in order to reduce stigmatization due to visible skin diseases. For an evidence-based approach, it is essential to obtain an overview of the existing literature to determine the need and plan for interventions, where necessary. Accordingly, it is the aim of this systematic review to compile a structured summary of the literature on internalized and external stigmatization due to hair loss.

Material and Methods

This systematic review was conducted according to the guidelines of *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) [14] and *Meta-Analysis of Observational Studies in Epidemiology* (MOOSE) [15]. Prior to execution, the underlying protocol was registered in the PROSPERO database for systematic reviews (registration number: CRD42019122966) [16].

Search strategy and selection process

The databases MEDLINE (PubMed), EMBASE, PsycINFO, and PsycNET were searched systematically by means of predefined search terms consisting of *Medical Subject Headings (MeSH-terms*) terms and other selected keywords. The following search terms were used: "*alopecia*", "*stigma*", and "*humans*", as well as corresponding alternative terms (Table 1). In addition, the source references of the full publications in the last stage of the selection process were manually searched for additional suitable publications. No time restriction was chosen (last update: May 07, 2019).

All identified articles were assessed by two independent reviewers (MS and LT; both MPH and PhD students). In phase I of the selection process, titles and abstracts were read and evaluated based on predefined criteria. In phase II, the full texts of those studies assessed as relevant during phase I were evaluated and reviewed with respect to inclusion and exclusion criteria (Figure 1). Discrepancies were discussed and, in case of disagreement, a consensus was reached in consultation with a third reviewer (AZ; PD Dr. Dr. med., MPH; senior physician). If the full text was not available, the corresponding author was contacted by e-mail.

Table 1 Conception of the used search term according to respective guidelines.

Core concepts	Concept 1	Concept 2	Concept 3	Concept 4
	Participants	Exposure	Outcome	Language
Keywords and MeSH terms used for search	– Adolescent – Adult – Aged – Child – Female – Humans – Male – Middle Aged – Young Adult	– Alopecia – Alopecia Areata – Alopecia Areata totalis – Alopecia Areata universalis – Alopecia Areata/epidemiology – Alopecia Areata/mental health* – Alopecia Areata/psychology* – Alopecia Areata/therapy* – Alopecia areolaris syphilitica – Alopecia/chemically induced* – Alopecia/psychology* – Alopecia/rehabilitation* – Androgenetic Alopecia – Bald Head – Bald – Effluvium – Frontal fibrosing alopecia – Hair Loss – Ophiasis – Postmenopausal frontal fibrosing alopecia – Telogen effluvium – Trichotillomania	– Internalised Stigma – Internalized Stigma – Perceived stigma – Self-Stigma – Social Stigma* – Stereotyping – Stigma – Stigma, social – Stigmata – Stigmatising – Stigmatisation – Stigmatization – Stigmatize	– English – German
Combined search term	(Adolescent OR Adult OR Aged OR Child OR Female OR Humans OR Male OR Middle Aged OR Young Adult) AND (Internalised Stigma OR Internalized Stigma OR Perceived stigma OR Self-Stigma OR Social Stigma* OR Stereotyping OR Stigma OR Stigma, social OR Stigmata OR Stigmatising OR Stigmatization OR Stigmatisation OR Stigmatize) AND (alopecia OR alopecia areata OR alopecia areata totalis OR alopecia areata universalis OR alopecia areata/epidemiology OR alopecia areata/mental health* OR alopecia areata/ psychology* OR alopecia areata/ therapy* OR alopecia areolar syphilitic OR alopecia/chemically induced* OR alopecia/ psychology* OR alopecia/ rehabilitation* OR androgenetic alopecia OR bald head OR bald OR effluvium OR frontal fibrosing alopecia OR hair loss OR ophiasis postmenopausal frontal fibrosing alopecia OR telogen effluvium OR Trichotillomania) AND ((english [language]) OR (german [language])).			

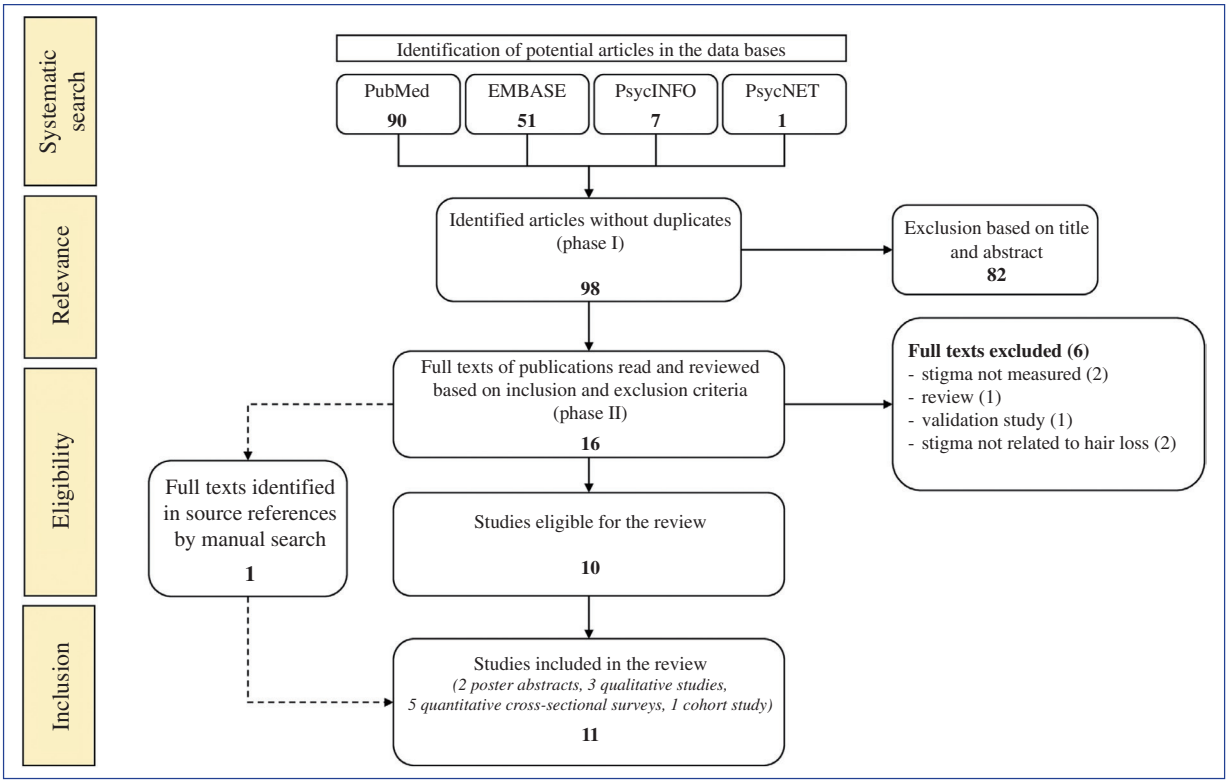

Figure 1 Flowchart with counts of the literature used at any time during the literature search.

Inclusion criteria

All study designs (quantitative and qualitative studies) were considered for this review. Studies were assessed as relevant during phase I and phase II if they (i) addressed external or internalized stigmatization of individuals with hair loss, or (ii) included health-related stigma due to hair loss as dependent or independent variable.

Exclusion criteria

Studies were excluded in phase II if they (i) were not available in the English or German language, (ii) consisted of an editorial, comment, or study protocol, (iii) did not present any own data, or (iv) addressed exclusively stigma not attributed to hair loss (for example, stigmatization due to gender, sexuality, or ethnic group).

Data collection and quality assessment

The data extraction and study assessment described below was performed independently by both MS and LT. Where present, the following data were extracted from each study: title, last name of first author, year of publication, type of article (full publication/abstract), study design, methodology and instruments of data acquisition, patient number, and collected outcome variables.

All included cross-sectional studies were assessed by two authors (MS, LT) with the checklist *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) [17]. Qualitative studies were assessed with the checklist *Consolidated Criteria for Reporting Qualitative Research* (COREQ) [18]. The development version of the STROBE checklist for conference abstracts was used to assess publications only available as abstracts [17].

The quality of a study was assessed based on the proportion of described subitems considered relevant and reported in the corresponding checklist: A (very good) > 80 %, B (good) 80–50 % and C (too inaccurate) < 50 % [19]. In case of discrepancy, the two quality assessments were discussed and, if no consensus was reached, AZ was included in the final decision. The *interrater* reliability between MS and LT was 54.5 %, and any disagreement could be resolved without assistance by AZ. Exclusion due to inferior quality of articles was not predefined.

Results

The systematic literature search in the four databases identified 98 publications. After exclusion of publications based on titles and abstracts, 16 articles remained for examination of

the full texts. Another study was identified by manual search of the reference lists in the inspected full publications. After evaluation of the full texts, eleven studies were included in this review (Figure 1).

The characteristics of the included studies and their associated authors are described in Table 2. The majority of the articles came from Europe (5/11) and Turkey (3/11) and were predominantly published in dermatological (5/11) and psychological (3/11) journals. The average number of authors per publication was 5.5, and most first authors were affiliated with a dermatological or psychological institution (36.4 % each). The median impact factor of the included scientific journals was 3.117 with a range from 0.884 to 8.017. The articles were published in ten different journals. Two of the identified articles were published in the *International Journal of Trichology* (Table 2). The included publications comprised two poster abstracts [20, 21], three qualitative studies [22–24], five quantitative cross-sectional surveys [25–29], and

Table 2 Overview over the characteristics of included articles and authors (n = 11).

General characteristics of the included articles			n (%)
Authors	Number of authors	1–3	3 (27.3)
		4–6	4 (36.4)
		> 6	4 (36.4)
	Countries of institutions of the respective first authors	Europe	5 (45.5)
		Germany	1 (9.1)
		France	1 (9.1)
		Netherlands	1 (9.1)
		Italy	1 (9.1)
		United Kingdom	1 (9.1)
		India	1 (9.1)
		Tunisia	1 (9.1)
		Turkey	3 (27.3)
		USA	1 (9.1)
Scientific journals	Topics of scientific journals	Dermatology	5 (45.5)
		Psychology	3 (27.3)
		Oncology	2 (18.2)
		Patient-centered medicine	1 (9.1)
	Titles of scientific journals	International Journal of Trichology	2 (18.2)
		Anais Brasileiros De Dermatologia	1 (9.1)
		British Journal of Dermatology	1 (9.1)
		Cancer Nursing	1 (9.1)
		European Journal of Cancer	1 (9.1)
		European Psychiatry	1 (9.1)
		Health Psychology	1 (9.1)
		JAMA Dermatology	1 (9.1)
		Journal of Investigative Dermatology	1 (9.1)
		Patient Education and Counseling	1 (9.1)
	Impact factor 2017 (median, range)		3.177 (0.884–8.107)

one retrospective cohort study, which, however, presented only a cross-sectional report on stigmatization [30]. Subdivided according to the pathogenesis underlying hair loss, five studies focused on therapy-induced hair loss (chemotherapy or endocrine therapy) [20, 22–24, 30], four on androgenetic alopecia [25, 27–29], three on alopecia areata [21, 25, 29], and one on diffuse alopecia [28] (Table 3).

Measuring instruments

The Hairdex [11] was used in four of the eight quantitative studies and thus the most frequently utilized instrument [25, 27, 28, 30]. It consists of 48 questions, such as "The condition of my hair impairs my societal and social life" or "The condition of my hair makes it more difficult for me to achieve as much as usual", and is specifically concerned with the impairment of the quality of life due to hair loss. The factor of stigmatization is evaluated with a subscale consisting of eight questions (Cronbach's α of 0.68 [11]). For each question, affected individuals assess on a five-step Likert scale to what degree statements such as "The condition of my hair is disfiguring me" apply to them. Subsequently, the achieved scores for both total scale and individual subscales are linearly transformed into a value range from 0–100 with higher values indicating more severe impairment.

Only three studies used measuring instruments specifically developed for measuring stigma. Specifically, the *Internalized Stigma Scale* (ISS, Cronbach's α for psoriasis: 0.65–0.78) [21], the *Feelings of Stigmatization Questionnaire* (Cronbach's α for alopecia areata: 0.93) [26], and a combination consisting of a modified Stroop test and two approach-avoidance tasks [29] were used. In one poster abstract, the measuring instrument used for the determination of stigmatization was not comprehensible [20]. The categorization of the measuring instruments with respect to assessment of internalized and external stigma is depicted in Table 4.

Alopecia areata and androgenetic alopecia

A study by Temel et al. [21] showed a significant correlation between stigmatization due to alopecia areata and both the *Dermatology Life Quality Index* (DLQI; r = 0.508) and general mental health measured with the *General Health Questionnaire* (GHQ; r = 0.329). The scores for internalized stigmatization measured with the ISS [31] were comparable to the scores of patients with acne vulgaris and higher than those of patients with vitiligo (59.5 vs. 59.5 vs. 51.7) [21].

In another study, patients with various forms of hair loss (54 % alopecia universalis, 18 % alopecia totalis, 26 % alopecia areata, 2 % androgenetic alopecia) and their partners were examined by a combination of a modified Stroop test and two approach-avoidance tasks to quantify internalized and external stigma. The results of this study indicate that patients with hair loss are affected more by internalized stigmatization while patients with psoriasis rather react to stimuli that imply external stigma [29].

A third study compared alopecia areata and androgenetic alopecia [25]. Although, based on the Hairdex, patients with alopecia areata report a lower impairment of their quality of life (57.0 vs. 68.4; p = 0.025), no statistically significant difference was found on the stigmatization subscale (4.7 vs. 5.6; p = 0.372). Overall, there was a correlation between disease duration of alopecia areata and a higher impairment of the quality of life due to stigmatization (r = 0.54; p = 0.001). In both groups, women seem to experience more stigmatization, although this finding was not significant [25]. Moreover, when directly compared to patients with psychiatric diseases, such as depression or anxiety disorders, patients with alopecia areata showed a higher degree of stigmatization (74.1 ± 23.5 vs. 52.0 ± 24.3; p < 0.01) [26].

According to a study by Sawant et al. [27] that addressed androgenetic alopecia exclusively in men, younger and less severely affected men were less impaired by stigmatization [Hairdex subscale: 13.2 vs. 13.9 and 13.0 vs. 13.9] [27]. Another study on women with diffuse or androgenetic alopecia showed that patients with a highly visible form of diffuse alopecia were more severely affected by stigmatization than those with mild alopecia (37.8 vs. 16). The perceived stigmatization of affected patients increased steadily with increasing severity of androgenetic alopecia (20.1 to 26.9) [28].

Therapy-induced alopecia

Approximately half of the studies (5/11) addressed hair loss induced either by preceding chemotherapy for various tumors [20, 22–24] or endocrine therapy for breast cancer [30]. The quantitative assessments showed that 30.4 % of the patients considered hair loss as the most distressing side effect and that loss of hair resulted in stigmatization with impaired social interactions in 45.8 % of the patients [20]. Moreover, Freites-Martinez et al. [30] observed a mean Hairdex score of 14.6 (± 17.0) on the subscale for stigmatization while the score for the total Hairdex was 25.6 (± 14.5). Quantitative studies indicated psychological stress due to stigmatization, too. For example, patients were cited with statements such as "*I think the worst thing that bothered me was people used to look at me and be sort of ''aah.'' And then they sort of say, ''for the grace of God it's not me''…*" (female patient, 61 years, England) [23]. The experienced stigmatization was also described by statements such as "*Our cultural environment extremely values women's [healthy] looks and it doesn't allow us to show ourselves as we are…*" (female patient, 59 years, Italy) [24]. Affected individuals often try to hide the occurring hair loss [22]. This was often done by

Table 3 Characteristics of included studies.

First author, year of publication, quality*	Reference	Study design	Subjects				Methods and results	
			Number of participants (n)	Type of hair loss	Percentage of female subjects	Mean age in years (range)	Measuring instruments[1]	Relevant results[2]
Baati et al. 2010 B	[20]	Quantitative cross-sectional study, questionnaire-based	24 participants	Chemotherapy-induced alopecia	44.8 %	45.9	– *Rosenberg's Self-Esteem scale* – Bruchon-Schweitzer's Body-Image Questionnaire (QIC) – Hospital Anxiety and Depression scale (HAD) – Brief cope	45.8 % of the affected individuals suffered from stigma due to hair loss impairing their social interactions. 30.4 % of the patients specified alopecia as the most distressing side effect of chemotherapy.
Freites-Martinez et al. 2017 C	[30]	Quantitative longitudinal study, only cross-sectional acquisition of stigmatization, questionnaire-based	112 participants (52 with information about stigmatization)	Alopecia induced by endocrine therapy	100 %	59.8 (34–90)	– classification of alopecia according to severity – Folliscope 2.8 hair density – Hairdex – response to therapy	The mean score on the Hairdex scale was 25.6 (± 14.5). The score on the stigmatization subscale was 14.6 (± 17.0).
Gonul et al. 2018 B	[25]	Quantitative cross-sectional study, questionnaire-based	138 participants	Alopecia areata (n = 56)	44.6 %	29.3	– Hairdex – a Turkish instrument for quality of life (TLQ)	No significant difference was found for the stigmatization subscale [4.65 vs. 5.60]. Women seemed to suffer more severely from stigma. Patients suffering from alopecia already for some time reported significantly higher stigmatization.
				Androgenetic alopecia (n = 82)	63.4 %	30.1		

First author, year of publication, quality*	Reference	Study design	Subjects				Methods and results	
			Number of participants (n)	Type of hair loss	Percentage of female subjects	Mean age in years (range)	Measuring instruments[1]	Relevant results[2]
Kacar et al. 2016 B	[26]	Quantitative cross-sectional study, questionnaire-based	82 participants, 40 with hair loss	Alopecia areata	35.0 %	28.4	– *Feelings of Stigmatization Questionnaire* by Ginsburg and Link	Patients with alopecia areata seem to be affected more severely by stigmatization than patients with psychiatric diseases.
Rosman 2004 B	[22]	Qualitative study, guideline-based	35 participants	Chemotherapy-induced alopecia	74.3 %	2 groups: 51.5 and 58	– explorative study – disease history – signs of fatigue – the topic of hair loss arose spontaneously	Affected individuals report of hiding and concealing their hair loss to avoid stigma.
Sawant et al. 2010 B	[27]	Quantitative cross-sectional study, questionnaire-based	37 participants	Androgenetic alopecia	0 %	N/A	– lifestyle indices – Hairdex – *Symptom Check List*-90-R (SCL-90-R) – *Stressful Life Events Scale*	Young men (15 to 25 years) [13.17 vs. 13.90] and less affected men [12.99 vs. 13.94] seem to be less affected by stigma.
Schmidt et al. 2000 B	[28]	Quantitative cross-sectional study, questionnaire-based	50 participants (44 with information about stigmatization)	Diffuse or androgenetic alopecia	100 %	42.3 (19–66)	– Hairdex – *Berne Coping Forms* – Short version of *Social Support Questionnaire*	Increased perception of stigmatization in female patients with highly visible compared to slightly visible diffuse alopecia [37.78 vs. 16.89]. In androgenetic alopecia, the perceived stigmatization is increasing with severity [20.08–26.89].

Continued

Table 3 Continued.

First author, year of publication, quality*	Reference	Study design	Subjects				Methods and results	
			Number of participants (n)	Type of hair loss	Percentage of female subjects	Mean age in years (range)	Measuring instruments[1]	Relevant results[2]
Temel et al. 2017 B	[21]	Quantitative cross-sectional study, questionnaire-based	150 participants, 50 with hair loss	Alopecia areata	N/A	N/A	– *Internalized Stigma Scale* (ISS) – *Dermatology Life Quality Index* (DLQI) – *Perceived Health Status* (PHS) – *General Health Questionnaire* (GHQ) – Acne Quality of Life Scale (AQOL)	The mean score on the Internalized Stigma Scale (ISS) of patients with alopecia areata was comparable with that of acne vulgaris and higher than that of patients with vitiligo (59.46 vs. 59.48 vs. 51.68). For patients with alopecia, a significant correlation was found between the scores on the ISS and both the disease-specific quality of life (DLQI: r = 0.508) and general health (GHQ; r = 0.329).
Trusson et al. 2016 C	[23]	Qualitative study, guideline-based	24 participants	Chemotherapy-induced alopecia	100 %	54 (42–80)	– effects of the cancerous disease on the body and interpersonal relationships – statements on hair loss, wigs, and baldness – narrative analysis – sociological approach	It seems that the visibility of cancer, expressed by the occurrence of hair loss, affects the interpersonal contact.

First author, year of publication, quality*	Reference	Study design	Subjects				Methods and results	
			Number of participants (n)	Type of hair loss	Percentage of female subjects	Mean age in years (range)	Measuring instruments[1]	Relevant results[2]
van Beugen et al. 2016 A	[29]	Quantitative cross-sectional study	150 participants, 50 with hair loss and 47 partners of patients	– 54 % alopecia universalis – 18 % alopecia totalis – 26 % alopecia areata – 2 % androgenetic alopecia	84.0 %	52.2	– modified Stroop test (attention bias, internalized stigma) – approach-avoidance tasks (behavioral bias, external stigma)	Individuals affected by alopecia seem to be preferentially affected by internalized stigma, while patients with psoriasis rather responded to stimuli originating from other persons indicating external stigma.
Schmitt et al. 2012 B	[24]	Qualitative study, guideline-based	20 participants	Chemotherapy-induced alopecia	100 %	53 (34–70)	– perceived effects of an accompanying program – effects of hair loss – interpretative phenomenological analysis	Therapy-accompanying programs supporting women in case of hair loss could help them deal better with the symptoms of hair loss.

Abbr.: N/A, not available.
*Quality: A > 80 %, B 50–80 %, and C < 50 % of the criteria of the respective guidelines met.
[1]Measuring instruments that address stigmatization are printed in bold.
[2]All results related to stigmatization due to hair loss were considered as relevant.
[3]In this publication, no measuring instrument for detection of stigma was identified.

Table 4 Measuring instruments used for the quantitative depiction of stigma and their dimensions in relation to stigmatization.

Instrument	Use	External stigmatization	Internalized stigmatization	Not clearly specified*
Hairdex	[25, 27, 28, 30]			X
Feelings of Stigmatization Questionnaire	[26]	X	X	
Internalized Stigma Scale (ISS)	[21]	X	X	
Modified Stroop test	[29]		X	
Approach-avoidance tasks	[29]	X		

*From the information provided in the literature, it is not possible to conclude whether internalized or external stigmatization is measured.

wearing a wig and was associated with positive statements such as "*I'd had enough sort of that I did get a wig which was great*." (Female patient, 61 years, England) [23]. In this context, an accompanying program for patients with therapy-induced alopecia was described as a potentially positive addendum for improving quality of life and minimizing internalized stigma [24].

Discussion

To our knowledge, this systematic review is the first work providing an overview of the evidence of stigmatization in individuals with hair loss. In the available literature, only eleven publications were assessed as relevant for this topic. Irrespective of the cause of hair loss, it is, however, evident that affected individuals frequently suffer from internalized and external stigmatization. With respect to internalized stigma, hair loss is comparable to acne vulgaris and psychiatric diseases, such as depression and anxiety disorders. Internalized stigma is, however, more pronounced than, for example, in vitiligo.

Due to the fact that hair loss may occur as a symptom of several diseases, based on various pathogeneses and with different severity, the identified studies were very heterogeneous [5]. When comparing the studies, it became evident that the reported diminished quality of life due to stigma, as measured by the Hairdex, varied not only between pathologies but also between study populations (alopecia areata: 4.7 [25]; diffuse alopecia: 16.9 to 37.8 [28]; androgenetic alopecia: 5.6 [25] to 20.1 and 26.9, respectively [28]). Based on these findings, patients with diffuse alopecia [28] and women [25] seem to suffer more severely from stigmatization. Furthermore, almost half of the studies addressed hair loss as consequence of an already existing and treated disease, that is, hair loss as side effect. Given that this aspect is important for interpretation of the study results, the corresponding results are discussed separately.

Measuring instruments

Most studies used the Hairdex developed by Fischer et al. (Table 3) [11]. Given that this is a scale for assessing the quality of life that measures stigmatization only as subscale, these results are difficult to compare with the *Feelings of Stigmatization Questionnaire* [26] or the ISS [21], which are specifically designed to assess stigmatization. While the overall construct of the Hairdex is validated by DLQI and GHQ, it should be taken into account that no comparable scale was used to measure stigmatization when interpreting the subscale for stigmatization. Furthermore, the Hairdex has only been validated in German, though it was also used in other languages. In addition, none of the included publications gave any information on the transformation of the scores for total scale or subscales to the value range of 0–100. The corresponding authors were contacted to clarify this aspect. Three of the four authors responded. One author confirmed transformation of the subscale [28], while two authors reported that they did not make any transformation [25, 27]. This reduces both the informative value and the comparability of the results, thus excluding direct comparison of the studies and adequate individual evaluation of the scores and in consequence immensely diminishing the informative value of this review. Furthermore, the statement "*So far, I have not been taken seriously at all by my physician*" within the stigmatization subscale implies a need of action with respect to recognition of the psychosocial burden by medical personnel. However, exact scores for this question were not reported.

With respect to the stigma-specific questionnaires, it should be noted that the ISS was developed for assessing stigmatization in psychiatric diseases and has not yet been validated in the field of dermatology. Within the present sample, however, it showed plausible scores and good internal consistency, in turn suggesting good reliability [21]. In addition, the *Feelings of Stigmatization Questionnaire* was utilized, a tool that has been used for skin diseases in the

past. While its subscales have been validated for patients with psoriasis and show good consistency [32], they have no proven quality in the two study groups of psychiatric diseases and alopecia. This must be taken into account when interpreting the results. Another measuring instrument was the combination of a modified Stroop test and two approach-avoidance tasks. These instruments are embedded in psychological behavioral research and are well suited to assess stigmatization and its nature – internalized or external – without using a questionnaire [29]. In summary, measuring instruments for both external and internalized stigmatization are covered in the literature. However, these are either not validated or not easily comparable due to the heterogeneity of the studies.

Hair loss as symptom

Overall, the scores for the subscale of the Hairdex questionnaire [11] vary strongly between both the various pathogeneses and the various study populations. According to these results, patients with diffuse alopecia (16.9–37.8) [28] and women (androgenetic alopecia, women vs. men: 6.4 vs. 4.2; $p = 0.078$) [25] are more severely affected by stigmatization. The comparability of the studies is, however, limited, given that cultural influences, differences in gender distribution, and uncertain methodology regarding the use of the Hairdex may have affected the study outcomes. For example, only in Turkey was more than one of the relevant studies conducted and published. In general, however, the results underscore the psychosocial burden that can be triggered by hair loss [4, 9, 33].

Therapy-induced hair loss – hair loss as adverse event

Only one study used the Hairdex for the quantitative analysis of therapy-induced hair loss [30]. The corresponding score for stigmatization was comparable with the scores for androgenetic alopecia [27] or slightly visible diffuse alopecia [28]. While the heterogeneity of the populations and the use of a modified and non-validated form of the Hairdex have to be taken into account again, the qualitative studies underscore the findings indicating a high burden due to stigmatization [22–24]. While qualitative studies also often indicate the perceived stigmatization due to stares of others, no quantitative studies on this aspect exist in the literature. Furthermore, there are no quantitative differentiations between tumor classes or strategies of how patients have dealt with stigmatization.

Limitations and integration into the general context

Possible limitations of this review are the low number of publications, a potential publication bias and the lack of studies on minors, although it is well-known that hair loss may also occur at this vulnerable age [34]. Furthermore, the quality of the included studies varied strongly, which may have affected the informative value of this review. However, we decided against retrospective exclusion of qualitatively poor studies, given that also these studies have a certain informative value and the available data are already limited. Given that all studies have been evaluated by scientists working in related disciplines and published in peer-reviewed journals with impact factor that are listed in the common medical databases, reliability of the data and an adequate standard may be assumed. Another aspect is the frequent measurement of stigmatization by means of the Hairdex, a questionnaire addressing quality of life [11]. While this is validated as instrument overall and well-accepted based on the frequent use, the informative value of the individual subscales – such as stigmatization – is not guaranteed. Furthermore, methodological information, for example whether the scores for the subscales were transformed into the standardized range from 0–100, is largely missing in the existing literature. If this aspect is viewed in connection with the large differences regarding the scores for the stigmatization subscale between studies (4.7 [25] to 37.8 [28]), it can be assumed that these have no quantitative informative value, either compared with each other or separately. Due to the lacking methodological details, these scores can only be regarded as a trend. Given that this strong limitation applies to four of the eight included quantitative surveys, however, this impairs the generalization of the presented results. Furthermore, these are the only four studies using the same tool for quantification of stigmatization and might, therefore, be useful for quantitative comparison.

In conclusion, individuals with hair loss suffer, irrespective of the specific cause, from internalized and external stigmatization resulting in massive impairment of their quality of life. Despite the resulting high psychological burden for the affected individuals, stigmatization is currently assessed only as one of many factors limiting the quality of life. Specific studies on the topic of stigmatization due to hair loss are rare; longitudinal studies do not exist, although they are strongly recommended. Additionally, methodologically high-quality and reproducible studies are needed that allow comparison between pathogeneses and with other diseases with visible changes are required in order to better assess the stigmatization and the high psychosocial burden caused by hair loss.

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